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ON TUMOURS OF THE MALE BREAST

SURVEY OF MATERIAL OPERATED ON IN FINLAND

BY

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Preface

The subject of the present investigation was suggested to me by Professor U. Uotila, M.D., in 1945, when the investigation was initiated. He has continuously followed the course of the work and supervised it with untiring readiness, giving important advice both on the theoretical planning of the research and on the practical methods of work. For all this I am greatly indebted to him.

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Visa Jääskeläinen

CONTENTS

Historical Introduction and Definition of the Object of the Present Investigation

Up to 1927 the prevailing conception appears to have been that the majority of tumours of the male breast were carcinomas. This is distinctly evident in the studies published by Schuchardt (1885—1891), Williams (1899, 1892), Poulsen (1890), Finsterer (1906), Speese (1912), Primrose (1913), Speed (1925), and Geldmacher (1926); their materials, it is true, also include sarcomas and beningn tumours, but mainly carcinomas.

Andrews & Kampmeier (1927), as a result of their investigations, were the first to maintain that mammary carcinomas in men are much more rare than the benign male mammary enlargements encountered. The same opinion was arrived at by Semb (1928), Horsley (1939), Geschickter (1943), and Word & Reed (1943). In addition, the main part of the materials of all these investigators consisted of non-neoplastic benign mammary enlargements, Andrews & Kampmeier's material even exclusively of them.

Although very different conceptions have prevailed regarding the quantitative relationship of malignant to benign male breast tumours, malignant growths as such have constituted a patho-anatomically well-defined group that can be distinctly established.

On the other hand, study of the patho-anatomic character of benign mammary tumours especially, and among them expressly that of the fibro-epithelial, and the patho-anatomic

definition of the different types has proved a fairly complicated problem, and contradictory views have been advanced.

Many investigators, such as Schuchardt, Williams, Poulsen, Keyser (1904), Rose (1936), v. Nanay (1941) have described the benign mammary tumours encountered by them in the male as different types of neoplasms. The commonest diagnoses have been fibroadenoma, adenofibroma, fibroma, adenoma, cystadenoma, cysta, papilloma, lipoma and angioma; less frequently, chondroma and myoma. Schreiner (1932) and Charache (1940), again, considered the major part of the benign fibro-epithelial tumours of the male breast examined by them to be non-neoplastic formations, terming a number of them, however, as fibroadenomas. On the other hand, Semb, Geschickter and Word & Reed held that the predominant part of the tumours of the male breast examined by them were diffuse, non-neoplastic formations, not a single case being classed as fibroadenoma.

In the last five of the above-mentioned materials, in addition, some cases of lipoma, papilloma and angioma were found. It seems that most of the investigators consider them as rare. — Furthermore, Schuchardt and Schreiner found a tuberculous process in the male breast, and the latter as well as Word & Reed a simple abscess.

Non-neoplastic, fibro-epithelial male breast tumours have been much investigated; varied opinions have been advanced on their character, and they have been described by a variety of names.

The term gynecomastia has been employed as a general name for such formations by Stieda (1895). Menville (1933), v. Numers (1933), Sullivan & Munslow (1942), Geschickter (1943) and Karsner (1946). — Stieda, Erdheim, Geschickter and Karsner consider gynecomastia as hyperplasia of the normal mammary gland of the male, Menville takes it as hyperplasia sometimes connected with mastitis, v. Numers and Sullivan & Munslow as Mastopathia cystica.

According to Bertels (1913), benign fibro-epithelial male breast tumours are of the same character as »Mastitis chronica cystica», and he applies this term to them. Consten's conception of the character of the cases investigated by him was that their most prominent feature was proliferation of connective tissue similar to that occurring in the involution of mammary gland visible in the female menopause, and he termed them »diffuse fibromatosis». But he assumed, on the strength of other investigators' results, that the male might have mammary tumours differing somewhat from these, viz. pure hyperplasias, to describe which he recommended the denominations, according to the patient's age, of »Mastitis pubescentium» or gynecomastia. — Bailey (1924) understood similar cases investigated by him as »chronic interstitial mastitis or diffuse fibroadenomatous hyperplasia». Andrews & Kampmeier advanced the opinion that benign fibro-epithelial breast tumours in the male were of an inflammatory character, and therefore termed them »Mastitis chronica». According to them, the same histological features were present to a lesser extent in the normal mammary gland of the male. In addition, they were the first to maintain that all benign fibro-epithelial breast growths in the male were of a similar patho-anatomical character. — Moszkowicz (1927) also studied both normal and enlarged mammary glands of the male; on the basis of his cases he divided the latter into two classes: gynecomastia and »Mastopathia senescentium». In his opinion, there was a difference of degree only between these three classes, the ramification of glandular ducts having increased in the above order. According to Moszkowicz, the main question, therefore, is one of a hyperplasia of the glandular ducts. Theoretically, he wanted to keep separate another group of mammary gland enlargements present in the age of puberty, which he termed »Mastopathia adolescentium». — v. Gusnar (1928) also studied both normal and enlarged mammary glands in the male, and described his latter cases as »diffuse mammafibrosis», in which according to him the connective tissue only had become hypertrophic. He made a distinction between this and gynecomastia,

which he assumed to represent, in the first place, hyperplasia of glandular tissue. — On the basis of his investigations Semb arrived at the result that, apart from papillomas — which were rare — all benign fibro-epithelial breast tumours in the male resulted from the same process, viz. »Fibro-adenomatosis cystica mammae», which he identifies with Reclus' disease. — Nathanson (1944) wished to consider the following three processes as differing somewhat from each another: »Mastitis pubescentium», gynecomastia and »Mastitis senescentium». However, he does not describe the character of the difference e.g. microscopical; he considered all of them as hyperplasia.

The conception of fibro-adenoma even has been differently interpreted by different investigators. — Consten, Semb and Moszkowicz have wished to emphasise the definition of fibro-adenoma: the two former claimed that a growth of this type must be distinctly demarcated against its surroundings by a capsule, and that it contains no fat cells; Moszkowicz pointed out that fibro-adenoma displays characteristic distorted figures (Verzerrungen) due to its mechanism of origin, the overgrowth of »mantle connective tissue»; Consten also pointed out that only fissure-shaped and never round cysts are seen in fibro-adenoma proper. If an attempt is made to review against this background the results of the investigators who have diagnosed male fibro-adenomas, it would appear that, as regards Poulsen's, Keyser's Rud's and Takahata's cases for example, not all of them correspond to the above definitions, particulary as regards the demarcation of the enlargements.

There is, therefore, a great deal of variety in prevailing conceptions of the character of the benign fibro-epithelial mammary enlargements of the male and of the terms employed. — This is neatly summed up by Tietze (1900) in his statement on a case investigated by him: »The enlargements, in exterior and consistency, were reminiscent of cystadenoma. But microscopic investigation revealed a diffuse disease of both mammae, reminiscent of fibro-adenoma . . .»

As ideas on the frequency relationship of malignant to benign mammary enlargements in the male have undergone great changes in the last twenty to thirty years and opinions on the character of benign fibro-epithelial tumours of the male breast have been very contradictory, it is of importance, from both the patho-anatomical and clinical point of view, that the character, symptoms, treatment and mutual relationship of these two groups are clarified. — Hence, the present investigation attempts to answer the following questions:

1. What patho-anatomical formations do male breast tumours represent, and what are the relative frequencies of the different types?

2. What more detailed observations can be made on the pathologic anatomy of the different types of tumours of the male breast?

3. From the observations made, can conclusions be drawn as to the etiology of the various tumours of the male breast?

4. What is the clinical picture of the tumours of different types of the male breast, and can they be classified on this basis?

5. How have the different tumours of the male breast been treated, what are the results of the treatment, and what therapeutic measures can be considered the most advantageous?

Material and Organisation of the Investigations

The material was collected by a methodical search for all patho-anatomical preparations of tumours of the male breast, irrespective of their diagnosis. 121 cases were obtained from the Department of Pathological Anatomy, University of Helsinki, 69 from the Central Institute of Radiation Therapy, University of Helsinki, 12 from the Finnish Red Cross Hospital in Helsinki, 10 from the Surgical University Clinic in Helsinki, 2 from the Patho-Anatomical Institute in Turku, one each from the Helsinki »Deaconess» Hospital, Kuopio County Hospital and Pori General Hospital. All the specimens were re-investigated, with the exception of a case of mammary carcinoma of which the specimen was untraceable. — However, of four of the cases in the material no microscopical preparation had been made; of them, two came from the Central Institute of Radiation therapy, one from Hatanpää Hospital and one personally from the physicians in charge of the case. One of them was a clinically distinct inoperable mammary carcinoma and one an equally obvious case of gynecomastia; neither of the two patients was operated upon but they were kept under observation in the therapeutic institute and the former was given radiation treatment. From the third patient a benign growth had been removed from the mammary gland, but as from macroscopic examination it looked like a lipoma, no microscopic examination was effected. The same applied to the fourth case, a bilateral gynecomastia, in whom a year later a testicular tumour was stated,

but in this case omission of the patho-anatomical examination was evidently in part due to the exceptional conditions of war-time.

Practically, the collected material therefore includes only cases examined patho-anatomically. Hence, the material contains no cases of »Mastitis neonatorum». — The entire material consists of 221 cases, of which the oldest date from 1903 and the freshest are those examined before the end of 1947; a single case dates from 1948, a mammary carcinoma which was included in the material because of the rare occurrence of the type.

The relevant hospitals and physicians were asked for more detailed clinical reports on the cases on the basis of data on examination records, and for the patients' addresses. All the patients that could be traced were sent a questionnaire, a specimen of which can be found at the end of this book. — The author has personally been in a position to effect both the basic and the follow-up examination of 5 patients, and a follow-up examination of 33 patients. The journals of the relevant hospital were traced in 126 cases. A written or verbal report by the physician in charge of the case was obtained for 20 patients. 53 of the patients answered the questionaire and in 3 cases their relatives for them. In 60 cases the clinical information is based only on the physician's report submitted with the specimen. — Table 1 gives the detailed sources on which the clinical information obtained on the patients is based.

Biopsy specimens fixed in the normal way in aqueous solution of 10 % formalin, submitted by the place of treatment for routine investigation, were generally used for patho-anatomical investigations. Generally, sections of 5 microns in thickness were made of them. The usual haematoxylin-v. Gieson staining was made of all the biopsy specimens, and haematoxylin-eosin staining from many of them. In addition, from all the malignant tumours available (22 cases), from 4 benign tumour specimens and from 58 specimens of gynecomastia, Harris' haematoxylin-eosin staining, methylene blue (½ % aqueous solution) and toluidine blue (1 % aqueous

TABLE 1. — SOURCES OF THE CLINICAL PICTURE

Type of clinical examination	Tumours		Gynecomastia
	Malignant	Benign	
Personal examination and hospital journal	5		19
Personal examination and description by the physician in charge		1	13
Patient's reply to questionnaire, and hospital journal	5		37
Patient's reply to questionnaire, and description by the physician in charge		1	10
Reply to questionnaire by patient's relations, and hospital journal			2
Reply to questionnaire by patient's relations, and description by the physician in charge	1		
Hospital journal alone	13	2	41
Description by the physician in charge, alone		5	63
Total	**24**	**9**	**185**

solution and 1 % solution in 60 % alcohol) stainings, and the Feulgen nucleal reaction with light-green contrast staining were made. In the methylene-blue and Feulgen stainings the sections, after removal of the paraffin, were kept in Zenker solution for half an hour, but otherwise R o m e i s's detailed instructions were followed in the technical execution of the stainings. — As new preparations were made in addition to all the old and faded stained preparations, several sections from different depths from practically every tissue sample fixed in formalin were examined. Furthermore, in a number of cases, two or several tissue samples of one and the same section were available, and they were all examined in the way described above.

When it was desired to investigate whether or not two phenomena observed in the material collected were interdependent, the so-called binomial distribution was studied according to L i n d e b e r g:

The mean error of the probability percentage P of each of the two phenomena studied,

$$\varepsilon P = \frac{100}{n} \sqrt{\frac{m(n - m)}{n}},$$

when n represents the total of cases in the material in question, and m expresses the number of cases in which the phenomenon to be studied is present. The mean error of the difference between P_1 and P_2, the probability precentages to be compared, is

$$\varepsilon (P_1 - P_2) = \sqrt{\varepsilon^2(P_1) + \varepsilon^2(P_2)}.$$

If the difference between the probability percentages to be compared is positive, and at least twice its mean error, it is very probable that the two phenomena studied are interdependent, and if the difference is at least three times its mean error, it is statistically absolutely certain that such interdependence exists (M a t t i l a; personal communication).

Pathological Anatomy of Mammary Tumours in the Male

Table 2 gives the materials by some investigators of tumours of the male breast, and to facilitate comparison, also the present Finnish material. — The table shows that with two of the investigators only, Schreiner and Rose, are the majority of the cases malignant tumours; against this, with five of the investigators the majority of the cases are gynecomastia, which term in the present paper will be employed to denote enlargements of the male breast that are not considered as neoplasms proper or inflammatory formations. It is true that, among the last-mentioned investigators, Andrews & Kampmeier give no other types of mammary enlargements in their materials, but their materials have been included as they were the first to emphasise that mammary enlargements of any other type are much less frequent in the male, though not denying their existence. — Further, it is noted that Schreiner, Geschickter and Word & Reed have found a few inflammatory mammary enlargements even in the male, although as a rarity.

As can be seen from the table the vast majority of the cases in the present material are gynecomastia, a good tenth are malignant tumours, less than a sixteenth benign growths proper, while only a few are inflammatory formations. The material, hence, differs from all the other materials given in the table, from most of them very distinctly, insofar as cases of gynecomastia are very numerous compared with tumours proper.

The difference between the materials in Table 2 in the quantitative relations of the different types of mammary enlargements seems to be due, in part, to the fact that certain

TABLE 2. — PATHO-ANATOMICAL TYPES OF TUMOURS OF THE MALE BREAST IN THE MATERIALS BY DIFFERENT INVESTIGATORS

	Tumours proper Malignant	Benign	Gyneco-mastia	Inflamm-ations	Total
Andrews & Kampmeier 1927			20		20
Semb 1928	8	4	40		52
Schreiner 1932	16	5	8	2	31
Rose 1936	14	4	3		21
Horsley 1939	4	7	23		34
Charache 1940	13	10	12		35
Geschickter 1943	33	4	108	5	150
Word & Reed 1943		2	15	3	20
Present material	**24**	**9**	**185**	**3**	**221**
	(11 %)	**(4 %)**	**(84 %)**	**(1 %)**	

investigators (at least Schreiner, Rose and Charache, Table 8) diagnosed fibro-adenomas among their material, and these consequently come in the group of benign tumours proper, while a number of the investigators mentioned in Table 2 advance no such diagnoses. This again may be due to the fact that the pathological anatomy of the benign fibro- epithelial mammary enlargements in the male has been interpreted differently; this aspect of the problem will be considered in greater detail later on. — In part, the differences in the conceptions of the investigators regarding the quantitative relations of the different mammary enlargements in the male obviously arise from the materials having been collected in different ways; for instance, Andrews & Kampmeier's material consists of cases encountered in

private practice, Semb's and Geschickter's of cases collected from a patho-anatomical research institute, Schreiner's, Rose's Horsley's and Charache's of civilian hospital patients, and Word & Reed's of military hospital patients. — The civilian hospital material no doubt gives an imperfect picture of the incidence of benign enlargements, particularly of gynecomastia, as they are often operated on policlinically; military hospital material, again, comprises many young patients. — A patho-anatomical research institute is unlikely to receive specimens of all cases of gynecomastia, as they sometimes seem so benign clinically that operation is not considered necessary; the benign tumours proper are probably operated on relatively more often than gynecomastia, since papilloma and angioma, for example, generally produce symptoms which necessitate their removal for corroboration of the diagnosis. — Materials from a practice, again, generally remain too limited to give a complete picture of the proportions of all the types.

As the present Finnish material contains practically exclusively cases examined patho-anatomically, it will probably provide a fairly true picture of the incidence of the malignant and benign tumours proper of the male breast, and also of that of inflammatory formations, whereas gynecomastia is likely to be somewhat more frequent in reality than the present investigation would indicate.

I. PATHOLOGICAL ANATOMY OF MALIGNANT MAMMARY TUMOURS IN THE MALE

1. Incidence of carcinoma and sarcoma

The best means of obtaining an idea of the incidence of the mammary carcinoma in the male is to take all mammary carcinomas diagnosed in a certain period of time in the same examination establishments and ascertain the percentage of instances in the male. — Table 3 shows that the results of foreign investigators have varied between 0.5 %—2 %, the arithmetical mean being 1.2 %. —In the present Finnish material the correspoinding ratio is 1.2 %.

It has been found, hence, that *mammary carcinoma in the male is nearly a hundred times less frequent than in the female,* and the present Finnish series no doubt reflects this proportion very well, the result yielded by it being very close to the mean of the results of other investigators.

Table 4 shows that the majority of malignant tumours in the male are carcinomas. In the foreign materials the relative amounts of carcinomas have varied in the range of 79 %—98 %, the arithmetical mean value being 89.3 %. The values in the four biggest series vary between 83 % and 98 %, the mean value being 92 %. — In the present Finnish material the percentage of carcinomas is 92.

The corresponding ratios for sarcomas, taking all the foreign materials into consideration, are within the range of 2 %—21 %, the arithmetical mean being 10.7 %; in the four biggest

TABLE 3. — MALE MAMMARY GLAND CARCINOMA PERCENTAGE OF ALL MAMMARY GLAND CARCINOMAS, ACCORDING TO DIFFERENT INVESTIGATORS

	Cases of mammary gland carcinoma		
	total	in the male	
		number	%
Williams	1879	16	0.9
Poulsen	330	5	1.5
Keyser	1416	10	0.7
Finsterer	692	11	1.6
Mülleder	612	12	2
Judd & Morse	1768	17	1
Schreiner	1240	15	1.2
Geschickter	2554	30	1.2
Kappelgaard	2547	13	0.5
Present material	**1190**	**13**	**1.1**

materials, 2 %—17 %, mean value 8 %. — In the present Finnish material the percentage of sarcomas is 8.

It can be seen, therefore, that, according to both the foreign materials and the present Finnish material, *approx. 9/10 of the malignant mammary tumours in the male are carcinomas and approx. 1/10 sarcomas.* This latter figure is considerably

TABLE 4. — CARCINOMA AND SARCOMA PERCENTAGES OF THE MALIGNANT TUMOURS OF THE MALE BREAST, ACCORDING TO DIFFERENT INVESTIGATORS

		Malignant tumours	
	Total	Carcinoma	Sarcoma
		%	%
Williams	19	84	16
Finsterer	14	79	21
Schreiner	16	94	6
Neal	60	83	17
Sachs	178	98	2
Geschickter	33	91	9
Kappelgaard	55	96	4
Present material	24	**92**	**8**

higher than the percentage of sarcoma of the malignant mammary tumours in the female, for which the following figures by some investigators may be given: Charache 0 %, D'Aunoy & Wright (1930) 0.1 %, Schreiner 0.3 %, Semb 1.1 %, Williams 4.8 %.

The fact that the incidence of malignant tumours in the male breast is considerably less than in the female is probably due to the atrophy of the former and to the absence of cyclic changes. Again, the fact that sarcoma is relatively more frequent among the malignant mammary tumours of the male than of the female is likely to be due to the predominant position of connective tissue in the male mammary gland. — In any case, these two features, the *numerical rarity of malignant tumours and the relative frequency of sarcomas, are characteristic of the male mammary gland.*

2. The different types of malignant mammary tumours in the male

The classification of carcinomas employed is that suggested by Castrén and generally adopted in Finland, according to which there are two main groups of carcinomas, covering and glandular epithelial carcinomas. The former are subdivided into plate, cylinder and intermediate epithelial carcinomas according to the predominant carcinoma cell type, the latter into adenocarcinomas and Carcinoma solidum, according to whether the carcinoma cells are capable of forming alveoli or not. In Carcinoma solidum, the forms alveolare and diffusum are distinguished, depending on whether the carcinoma cells are in distinctly defined groups or mainly occur singly; Carcinoma solidum diffusum has the subspecies simplex, medullare and scirrhosum, according to the amount of connective tissue. — Many investigators have employed different classification systems for carcinomas, and an attempt has been made to convert their results, as far as possible, to comply with Castrén's classification. The results both of other investigators and of the present, to facilitate comparison, are given together in Table 5. Table 6 gives in greater detail the carcinoma and sarcoma types of the Finnish material (Photos 1—9).

According to Table 5, both in the foreign materials and in the present Finnish material, *carcinomas of solidum type are*

TABLE 5. — PERCENTAGES OF THE DIFFERENT TYPES OF CARCINOMA OF THE MALE BREAST IN THE MATERIALS BY DIFFERENT INVESTIGATORS

	Total of cases in the material	Carcinoma of the male breast				
		Carcinoma solid. %	Adenocarcinoma %	Covering epithelium carcinoma %	Carcinoma Paget %	Carcinoma gelatinos. %
Mülleder	12	17	25	8		
Schneller	86	76.7	8.1	10.5		1.2
Wainwright	78	70.7	17	9		3.7
Schreiner	12	92	8			
Gilbert	42	64	21	2		
Neal	50	76	6	16		2
Sachs	178	37.6	40.7	0.56	1.12	0.56
Geschickter	30	53	36	10		
Kappelgaard	53	72	28			
Present material	**21**	**62**	**19**	**14**	**5**	

TABLE 6. — PATHO-ANATOMICAL TYPES OF MALIGNANT TUMOURS OF THE MALE BREAST IN THE PRESENT FINNISH MATERIAL

Patho-anatomical type	Number
Carcinoma solidum	2
—»— —»— alveolare	6
—»— —»— simplex	1
—»— —»— medullare	2
—»— —»— scirrhosum	2
Adenocarcinoma	4
Carcinoma spinocellulare	2
—»— basocellulare	1
—»— Paget	1
Fibrosarcoma	2
No microscopic examination	1
Total	**24**

as a rule in the majority, with adenocarcinomas holding the second place. The most remarkable exception is constituted by the biggest material of male mammary carcinomas found in the literature, that by S a c h s, which contains slightly more adenocarcinomas than cases of Carcinoma solidum. — *The covering epithelium carcinoma, as a rule, is third in order of incidence.* — The present Finnish material contains one case of Carcinoma Paget, reported only by S a c h s among the foreign investigators mentioned in Table 5. — Furthermore,

it is noted that the present material includes more carcinomas that originated with certainty in the covering epithelium than does any other series reviewed in this connection, with the exception of Keyser's material.

The two sarcomas in the present Finnish material are fibrosarcomas.

3. Feulgen reaction, basophilia of cellular cytoplasm and metachromatic stainability of tissues in male malignant tumours

In histological investigation, too, the continuous endeavour has been to elucidate the chemism of the tissues. For instance, Caspersson & Santesson (1942) have investigated the cells of normal and tumour tissues by special cyto-chemical analysis methods, by means of which the protein and nucleic acid content of individual cell parts can be established, and by comparing the results thus obtained with certain stainings. They found that an increase in the ribose polynucleotides content of cellular cytoplasm is characteristic of rapidly growing tissues, of cells where active formation of cytoplasm protein is in progress, and particularly of glandular cells producing protein. They also found that carcinoma tissue is built up of cells differing very greatly from one another in chemical and cytological structure; however, all the carcinoma cells can be arranged into a series according to the degree of activity of their protein formation system, from the actively growing cell, type A, which usually represents a minor part only of the cells of the tumour, up to the non-growing cell, type B. The nucleus of a cell of type A contains plenty of ribodesose polynucleotides and the cytoplasm plenty of ribose polynucleotides, the nucleus of a type B cell only little or no ribodesose polynucleotides and the cytoplasm little or no ribose polynucleotides. — In addition, Caspersson & Santesson found that the Feulgen reaction qualitatively but not quantitatively gives the ribodesose polynucleotides of the nucleus with fair specificity, and that the ribose polynucleo-

tides content of cellular cytoplasm is also expressed in basophilia of cytoplasm and the increase of ribose polynucleotides content in increased basophilia. — Lison (1935) found that the red colour resulting from the use of a certain toluidine blue staining method, »genuine metachromasia», is an expression of a reaction between ester sulphuric acids and the stain, and will therefore remain only in those parts of the tissue containing ester sulphuric acids. — Sylvén (1941. 1945) found that by estimating microscopically the intensity of the metachromatic colour and the number and granule content of the mast cells, the amounts of free and bound chromotropic component can be quantitatively estimated, provided all the preparations are treated in the same way. He also came to the conclusion that the granules of the mast cells probably contain heparin. By means of this metachromasia reaction he found that high molecular ester sulphuric acids are constantly encountered in great quantities in the connective tissue of the adult organism only in biological conditions where the new formation of connective tissue is in progress, i.e. in slightly differentiated, growing granulation tissue.

Investigation of the carcinoma and sarcoma preparations of the present material was effected by Feulgen reaction to determine the ribodesose polynucleotides of the nuclei, by methylene-blue staining to estimate the basophilia of cellular cytoplasm and by toluidine-blue staining to ascertain the metacromasia of the tissues. These investigations showed that the *Feulgen reaction as a rule revealed no great changes in intensity in cases of carcinoma*, but was fairly even in the majority of the preparations (18 out of 20), relatively strong in the majority (15 out of 20) also, and weak in only a few (5 out of 20). However, it is to be borne in mind that, as pointed out by Caspersson & Santesson, the Feulgen reaction cannot be used quantitatively; whether this is due to the formalin fixation of the biopsy specimens employed both in their material and the present, is difficult to say. — In the methylene blue staining of the carcinoma preparations of the present material it was observed that in the majority of the cases (13 out of 20) the basophilia of the cytoplasm of car-

cinoma cells apparently in active growth is greater than of those in a state of rest or regression. In six preparations (out of 20) the basophilia of the cytoplasm of the carcinoma cells in the entire sample was relatively even and strong, and in them the carcinoma cells were dispersed in small groups and seemed to be growing actively and infiltrating; of these, two were Ca spinocellulare, one Ca solidum medullare partim alveolare, one the beginning of an adenocarcinoma and two lymph nodule metastases of Ca solidum. In one preparation out of 20 the basophilia of the carcinoma cells was weak throughout (Ca solidum medullare). — The result, therefore, was that *in a total of 19 of the 20 investigated cases the basophilia of the cytoplasm of the carcinoma cells and, hence, the ribose polynucleotides content, seemed to be connected with the activity of these cells.* In an adenocarcinoma just beginning, in which the basophilia of carcinoma cells was fairly even and distinct, it could be noted, furthermore, that the basophilia of the cytoplasm of the healthy glandular duct cells in the preparation was distinctly stronger than that of the carcinoma cells. — The observations made in the present investigation on the basophilia of the cytoplasm of carcinoma cells is in keeping with the observations by Caspersson & Santesson, who stated that actively growing A cells, distinctly basophilic in their cytoplasm and containing plenty of nucleotides, are found in the carcinoma tissue mainly in the periphery, and that on the other hand the basophilia of the cytoplasm is particularly intense in glandular cells producing protein. — From preparations stained by toluidine blue to investigate the »genuine metachromasia» it was observable that *in the majority of carcinoma cases (18 out of 20) there was no or very little free metachromatic substance or mast cells,* and only in two carcinoma preparations were these substances more abundant: in a Carcinoma Paget and a Carcinoma solidum alveolare case, in which some free metachromatic substance and mast cells existed in the environment of the tumour cells. This, according to Sylvén and Lison, means that, generally, no high molecular ester sulphuric acids or heparin have been present in the investigated

tissues. Hence, the present observations comply with those of Sylvén and his finding that large amounts of free metachromatic substance and mast cells are present only in growing, slightly differentiated connective tissue, and therefore it was not to be expected that they would be found in any abundance in connection with epithelial tumours.

In one of the two sarcoma cases included in the present material, the nuclei assumed a distinctly violet colour in the Feulgen reaction, while the cytoplasm of the tumour cells proved only slightly basophilic with methylene blue; in the other case again the nuclei did not colour at all in the Feulgen reaction, while the cytoplasm of the tumour cells proved, generally, distinctly basophilic. — In none of the two cases did any free metachromatic substance or mast cells appear in toluidine blue staining. — Conclusions can hardly be drawn on the basis of these two sarcoma cases, at least not regarding the results of Feulgen reaction or methylene blue staining, which are contradictory in these cases. As regards the result of the metachromasia reaction, reference can be made to Sylvén's observations, according to which the cytoplasm and intercellular medium of fibrosarcomas contained free metachromatic substance and plenty of mast cells only when progressive growth was present in the parts investigated. It is possible, therefore, that in the parts of the sarcomas investigated here the tissue has not been actively growing.

II. PATHOLOGICAL ANATOMY OF BENIGN MAMMARY TUMOURS IN THE MALE

Benign tumours proper in the male breast are fairly rare, as can be seen from Table 7; this table gives materials by different investigators, and, to facilitate comparison, the present Finnish material as well, shown in greater detail in Table 8.

A closer study of Table 7 reveals that e.g. adenoma and cystoma are present in the oldest statistics, by Williams, but not in the statistics of a single later investigator. — This may indicate that the grounds for Williams's diagnosis as regards the tumours mentioned differ from those applied by the other investigators, and that such appellations would possibly not be used today for similar formations. — Poulsen's material, again, includes two fibromas, while none were found by any of the other investigators included in the table. Poulsen does not describe his fibromas in sufficient detail to allow of an opinion to be formed subsequently. But Geldmacher (1926), who has published a male mammary fibroma described in great detail, points out that it is very rare in the male. — And it has in fact been impossible to find mention of any other fibromas in the literature than the cases reported by him and Poulsen. — It may be mentioned that two of the benign growths in the present Finnish material were first diagnosed as fibromas but re-examination indicated that they were most probably fibrolipomas (Table 8).

As regards fibroadenomas, the different investigators have obviously had contradictory conceptions. — Schreiners's, Rose's and Charache's materials contain both fibroadenomas and gynecomastia (cf. also Table 2), v. Nanay again

TABLE 7. — NUMBER OF THE DIFFERENT TYPES OF BENIGN TUMOURS IN THE MATERIALS OF TUMOURS PROPER OF THE MALE BREAST

Investigator	Total of tumours	Including benign tumours									
		Adenoma	Fibroma	Fibro-adenoma	Papilloma	Cystoma	Cysta	Angioma	Lipoma	Fibro-lipoma	Total
Williams	25	1				1		1	1		4
Poulsen	7		2								2
Semb	12				1			1	1		3
Schreiner	21			1	1		1	1	1		5
Rose	18			4							4
Charache	23			7	1		1		1		10
v. Nanay	16			4	1						5
Geschickter	37				1		1		2		4
Present investigation	**33**						**1**	**2**	**4**	**2**	**9**

has no gynecomastia. — Semb emphasised particularly that benign mammary enlargements in the male, apart from papillomas, are not tumours in their character and, therefore, cannot be termed fibroadenomas. Menville (1933) was of the same opinion as he could not detect a difference microscopically between male mammary enlargements previously considered as fibroadenomas and those held to be gynecomastia. — Geschickter also shared Semb's and Menville's

TABLE 8. — PATHO-ANATOMICAL TYPES OF BENIGN TUMOURS IN THE MALE BREAST IN THE PRESENT MATERIAL, ACCORDING TO THE PRESENT AND ORIGINAL EXAMINATION

Patho-anatomical diagnosis arrived at in the present investigation	Number of cases	Differing original patho-anatomical diagnosis
Angiofibroma	1	
Haemangioma	1	
Fibro-lipoma	2	Fibroma durum Fibroma
Lipoma	3	
Cysta dermoides	1	»Granulating cavity»
Macroscopic patho-anatomical examination only	1	
Total	**9**	

opinion, although he wished to concede that if fibroadenomatous hypertrophy develops into a node of which the demarcation can be distinctly palpated, it might be justifiable to term it fibroadenoma. However, K a r s n e r, in contradiction, pointed out that the gynecomastia material investigated by him, which is the most extensive found in the literature, did not include a single case that could be considered as fibroadenoma. — The present material includes all the traceable patho-anatomical preparations of tumours of the male breast examined in Finland up to the end of 1947, and they do not include a single benign fibroepithelial enlargement that could be considered as a tumour proper, taking fibroadenoma as defined by e.g. C o n s t e n, S e m b and M o s z k o w i c z (cf. p. 10). — It seems, therefore, that if so accurate a definition of fibroadenoma is insisted upon in investigating mammary tumours, not many real fibroadenomas will be found in the male breast.

Hence, it has been concluded that *benign growths proper are rarely found in the male mammary gland, and, of such growths pure fibromas are extremely rarely found, and fibroepithelial growths other than papillomas hardly at all.*

III. INCIDENCE OF INFLAMMATORY CHANGES IN THE MALE BREAST

Inflammations proper are extremely seldom found in the male breast, if the cases termed »Mastitis chronica» by certain investigators are disregarded; they will be discussed in greater detail later. — Table 9 gives the cases found in the literature, and the cases encountered in Finland.

The table shows that tuberculosis of the male mammary gland has been reported more often than other inflammations of the male breast. Its incidence compared with tuberculosis of the female mammary gland is indicated by the material collected by Morgen (1931) from the literature: out of a total of 439 cases, 20 or 0.4 % occurred in the male. And the Finnish tub. mammae material by Klossner (1944), for instance, of 50 cases, included not a single occurrence in the male. — Sometimes a simple inflammation has been observed in the male breast, and sometimes an obvious abscess, as is shown in the table.

The total of inflammations proper of the male breast in the entire material of mammary gland enlargements presented by Schreiner amounted to 7 %, by Geschickter to 3.3 %, and by Word & Reed to 15 % (cf. Table 2).

In collecting the present Finnish material no inflammatory formations proper in the male breast were found, apart from the three cases reported in Table 9; however, it is possible that biopsy specimens have not been submitted for all the mastites treated. *These cases represent 1.4 % of the total material, or less still than the benign growths proper*, which accounted for 4.1 %. — One of these inflammatory cases, an

TABLE 9. — INFLAMMATIONS PROPER OF THE MALE MAMMARY GLAND.

	Tbc	Abscessus	Mastitis	Chancre	Actino-mycosis
Schuchardt	2				
Morgen	20				
Schreiner	1				
Geschickter		1	3	1	
Word & Reed		3			
Present material	**1**	**1**			**1**

actinomycosis mammae, which was verified bacteriologically, is so rare in the male breast that no mention of any other such case has been found in the literature.

The present publication does not intend to deal with the pathological anatomy of the inflammations proper of the male breast at any greater length, and will omit altogether their clinical properties, as the purpose was solely to give an idea of the percentage they represent of male mammary gland enlargements. Bearing in mind the fact that, e.g. the majority of the series in Table 2 contain no inflammatory formations at all, the frequency figure of the present Finnish material, 1.4 %, considering that the statistics are reasonably extensive, is likely to be quite close to the truth.

IV. PATHOLOGICAL ANATOMY OF GYNECOMASTIA

As previously mentioned in the historical introduction, many different conceptions have been advanced on the fundamental patho-anatomical character of the chronic fibro-epithelial tumours of the male breast, and they have been given varying names. — This is also obvious from the variety of diagnoses employed in the original patho-anatomical investigation of the cases of gynecomastia of the present Finnish material (Table 10). The different patho-anatomical diagnoses total 12, and in over one-third of the cases was the diagnosis something other than gynecomastia (69 cases); in half of the latter (35 cases), the diagnosis was Mastpathia cystica or Fibrosis mammae, in the other half again (34 cases) a benign neoplasm proper (fibroadenoma, adenoma, fibroma.).

Certain investigators, e.g. Consten, Moszkowicz and Nathanson, as reported in the historical survey, have maintained that not even all the diffuse benign fibro-epithelial mammary enlargements in the male are identical patho-anatomically, but that they differ somewhat in type according to the age of the patient. For this reason, it has been considered useful here to study whether the present material displays any difference in the histological qualities of the gynecomastia of the patients of different age classes, and all the collected benign fibro-epithelial mammary tumours in the male are given in Table 11 according to the age of the patients, thus illustrating the incidence of all the most important histological properties in the different age classes. — This table shows that practically all the histological features considered are seen, firstly, by age groups, secondly, in the same numerical

proportion as the breakdown of cases in the age groups. In other words, the microscopic picture of the benign fibro-epithelial tumours in the male breast, judging by the present material, is essentially the same in all age groups, and these tumours cannot be subdivided into types according to the age of the patients.

TABLE 10. — THE ORIGINAL PATHO-ANATOMICAL DIAGNOSES OF THE PRESENT FINNISH GYNECOMASTIA MATERIAL

Gynekomastia		114
Differing original patho-anatomical diagnosis:		69
Mastopathia chron.cystica	33	
Fibrosis mammae	2	
Fibroadenoma pericanaliculare	10	
Fibroadenoma	10	
Fibroadenoma simplex	3	
Adenofibroma	3	
Adenoma mamme	1	
Fibroma	4	
Gynekomastia. Fibroadenoma pericanaculare	1	
Gynekomastia. Fibroadenoma simplex	1	
Gynekomastia. Fibroma mammae	1	
No patho-anatomical examination		2
	Total	**185**

Table 11 shows, further, that, apart from one case, fat cells were found in all the microscopic preparations studied. — On the other hand, it can be established that, microscopically, no evidence of a capsule surrounding the formation was found in a single instance in the present material of benign fibro-epithelial tumours of the male breast, and that the operation records make no mention of a capsule having been observed macroscopically. — Nor has a peri- or intracanalicular type of growth been observed in the microscopic preparations. — Hence, provided Consten's and Semb's definition of fibroadenoma (p. 10) is applied, not a single benign fibro-epithelial tumour of the male breast in this material can be considered as fibroadenoma (as mentioned previously, p. 29).

TABLE II. — PROPERTIES OF THE GYNECOMASTIA CASES IN THE PRESENT MATERIAL.

	Age of patients, years									Total
	10-19	20-29	30-39	40-49	50-59	60-69	70-79	82	Unknown	
»Fibrous» connective tissue: generally scant in cells	11	41	15	11	12	10	7	1	7	115
—»— rich in cells	11	16	8	4	9	12	6		10	76
hyalinised: in part	3	12	7	4	7	7	3		6	49
to a great part	10	24	8	6	8	12	7	1	8	84
»Mantle connective tissue» —, ±	10	22	10	4	3	4	3		2	58
+, ++	12	35	13	11	18	18	10	1	15	133
Fat tissue —		1								1
+	22	56	23	15	21	22	13	1	17	190
Glandular ducts: generally sparse	4	15	4	3	4	2	3	1	2	38
—»— dense	18	42	19	12	17	20	10		15	153
—»— small	2	4	5	1	1	2	1		3	19
—»— medium-sized	20	52	18	13	20	16	12	1	13	165
—»— large		1		1		4			1	7
Cysts +	19	46	20	13	21	20	12	1	13	165
Lobuli +	2	9	3	2	1	3	1		4	25
Glandular epithelium: generally 1-layered		5	5		1		2			13
—»— 2 —»—	22	52	17	15	20	22	11	1	16	176
—»— 3 —»—			1						1	2
Glandular epithelial cells: generally flat	2	1				3				6
—»— cuboidal	13	40	15	11	17	16	8		15	135
—»— cylindrical	7	16	8	4	4	3	5	1	2	50
Epithelial proliferation	10	31	10	8	9	8	4		7	87
Papilloma in a small duct		2	2		1					5
Secretion in the ducts	15	38	15	13	15	21	8	1	12	138
Epithelial desquamation	12	22	6	9	7	8	3		6	73
»Pale epithelium»	2	7	3	1	2	1			3	19
»Intermediate epithelium»		5	3		1	1			1	11

Apocrine sweat glands	1	4		1	2	6	4		3	21
Inflammation cell infiltration: scant	19	47	22	13	17	19	10	1	15	163
moderate	3	9	1	1	4	3	3		2	26
fairly abundant		1		1						2
Total of preparations *)	**22**	**57**	**23**	**15**	**21**	**22**	**13**	**1**	**17**	**191**

As will be reported in greater detail in the chapter dealing with the etiology of gynecomastia, several investigators, e.g. Andrews & Kampmeier, Erdheim (1928), Semb, v. Numers, and Sullivan & Munslow, in their gynecomastia material, did not find a single case where the etiology was a distinctly ascertainable hormonal factor, and in the present Finnish material the number of cases in which such an etiology can be presumed possible is only 8 out of 78. However, certain investigators have described individual cases of gynecomastia where the etiology seems to have been hypoplasia of the testes or anorchism, a testicular tumour, adrenal disorder, pituitary tumour or stilbestrol medication. Among them, Moszkowicz, and in addition to him Consten and v. Gusnar, although they themselves had no such cases, have advanced the assumption that gynecomastia cases of this type are patho-anatomically different from the others, or from the majority of gynecomastia cases. — A study of the microscopic descriptions of such individual cases of gynecomastia, published e.g. by Stieda, Bailey, Cairns, Moszkowicz, Heidrich & al., Edwards & al., Staemmler and Moore & al., however, shows that no distinct uniformity on the one hand, and on the other no features differing essentially from the histological properties of gynecomastia observed in the present investigation and given in Table 11, are to be found in the cases under reference. Nor does the microscopic picture differ in any way from the histology of the gynecomastia cases in the present Finnish

*) The total of patients is 183, including 8 for which, in addition to the first preparation, another biopsy specimen was prepared in connection with a relapse or gynecomastia appearing subsequently in the other breast.

material, even in the seven cases of the material where the patients displayed hypoplasia of the testes, or in the case where the patient had received stilbestrol immediately prior to the appearance of gynecomastia. — On the basis of the foregoing it would seem, therefore, that gynecomastia present in connection with testicular affections and other diseases of the endocrine glands is patho-anatomically essentially similar to other cases of gynecomastia.

Generally, the conclusion may be permitted that, *apart from duct papillomas*, which obviously have been found in the male mammary gland (Table 8) although not in the present material, *all or at least the majority of the benign mammary gland tumours in the male are diffuse formations and similar in their patho-anatomical character*. Hence, it would be both justified and reasonable to employ the same denomination for all of them.

1. Properties of glandular epithelium and the mutual relations of the different types of epithelial cells in gynecomastia

The glandular epithelium of the normal mammary gland of the male is, according to the investigations of Andrews & Kampmeier a 1-layered cylindrical epithelium, according to Erdheim 2-layered regular, and according to Karsner 2- or 3-layered and never a papillarily proliferating epithelium. v. Gusnar made a thorough examination of the normal mammary glands of males of different ages, and according to him the glandular epithelium at a young age is 2-layered, the cells of the layer being cylindrical, the basal ones flat; at a more advanced age the epithelium is often simple as the basal layer of cells is generally absorbed in the hyalinised basal membrane, and the cells are generally flatter. v. Gusnar found that »pale epithelial cells» in groups were often present between the cells of the inner epithelial cell layer; he considered them as sweat gland cells. He also reported often having seen direct inter-

mediate forms between mammary gland and sweat gland cells. Furthermore, he found that at the age of puberty the epithelium often revealed real proliferation phenomena.

The epithelium of gynecomastia, according to Andrews & Kampmeier, is simple, according to Moszkowicz and Semb 2-layered, according to v. Numers stratified in two or several layers, according to Karsner 3-layered and according to Erdheim stratified in several layers. In shape the epithelial cells, according to Stieda, Andrews & Kampmeier and Semb, are cylindrical, and according to v. Numers and Karsner cuboidal and sometimes cylindrical. Bertels, Consten, Moszkowicz. Erdheim, Semb, Menville, v. Numers, Geschickter and Karsner found proliferation in the epithelium of gynecomastia which, according to the last five of these investigators, could sometimes form papillomatous projections into the lumen of the ducts. Menville and Karsner even found desquamated epithelial cells in the lumen of the ducts fairly often. Semb stressed that there generally is a distinct basal membrane in gynecomastia. He also emphasised that no »pale epithelium» had been observed in this cases. v. Numers, on the contrary, found it in a couple of his cases, and Karsner in some of his. Semb, v. Numers and Karsner considered the »pale» epithelial cells to be formations related to the apocrine sweat gland cells, and on the other hand they found them to be present in abnormal involution of the female mammary (Mastopathia cystica). It may be pointed out here that Berning & Bücker (1937) in their investigations found that the »pale epithelium» was also fairly regularly present in the clinically normal female mammary.

On the basis of the above investigations it would seem that proliferation phenomena are fairly often present in gynecomastia, whereas in the normal mammary of the male they occur relatively seldom. This is obvious also from the fact that in some investigations the epithelium in gynecomastia has been found multilayered, but the epithelium of the normal mammary of the male 2-layered or simple. — Regarding the shape of the

epithelial cells both in gynecomastia and the normal mammary of the male, and the number of layers of epithelial cells in gynecomastia, the various investigators have made somewhat differing observations; two investigators only have found »pale epithelium» in their cases of gynecomastia, and one, v. G u s n a r, in the normal mammary glands of the male. — Of particular interest is the observation by v. G u s n a r that the normal mammaries of the male quite often contained epithelial cells that seemed to be direct intermediary forms between mammary gland and sweat gland cells, to such a degree that it had often been difficult to distinguish which of the two were in question. It has not been possible to discover any further mention in the literature of such cells having been found in the normal or enlarged mammary of the male, except for the detailed description by v. N u m e r s of one of his cases, although he did not emphasise the exceptional nature of the epithelium he described.

It was found in the present investigation (Table 11) that *in some 90 % of the gynecomastia preparations the epithelium of the glandular ducts was as a rule 2-layered.* In some preparations it has generally been simple, and, moreover, the epithelium of most of the small glandular ducts belonging to the lobules, the acini, was simple. In two preparations only was the epithelium generally 3-layered. — In almost half the gynecomastia preparations *proliferation of the glandular duct epithelium* was established microscopically (Photo 15, 16) when, in a smaller or larger part of the glandular ducts of the preparation, the epithelium was multilayered but uneven, the number of layers varying both within an individual duct and between the different ducts. Sometimes it has been difficult to decide whether the basic form of the epithelium was 2- or multilayered. — In five preparations only had the proliferation of the epithelium produced a *papilloma* in a small glandular duct (Photo 17). But *not one instance of intracanalicular growth was observed.* — *Desquamated epithelial cells* were found in some 40 % of all the preparations. — The *basal membrane* was distinct in all of them. — The *shape of the glandular epithelium cells* was cuboidal in approx. 70 %

of the preparations of the present material, and cylindrical in approx. 25 %. A flat epithelium, on the other hand, is rare as the general epithelial shape of the preparation, and is found mostly in major cysts.

Of the gynecomastia preparations in the series, »*pale epithelium*» was found in 19 (Photo 18). The cells of this epithelium are very high, cylindrical, fairly varying in length, and they have oblong nuclei, generally situated in the central part of the cell. The cytoplasm does not stain with haematoxylin-eosin and haematoxylin-v. Gieson methods, but remains »pale». It was also established that the cytoplasm of the »pale cells» would not stain with methylene blue even, and hence it has no basophilia and therefore also no considerable amounts of ribose polynucleotides. These cells generally form one layer, but proliferate fairly often; »basket cells» are sometimes seen at their base. The glandular ducts with »pale epithelium» are situated in the ordinary connective tissue of the mammary gland, and generally in the middle of the mammary gland ducts.

Among the 19 preparations revealing a »pale epithelium», 7 also displayed an epithelium of peculiar appearance that looked like an *intermediate form* between the »pale» and the normal mammary gland epithelium (Photos 19, 20). This epithelium has one layer of cylindrical cells which are nearly as high as the »pale» epithelial cells; they have oblong nuclei, often possess beautiful basket cells at the base, and their cytoplasm stained with haematoxylin-eosin and haematoxylin-v. Gieson methods in the same way as that of the ordinary mammary gland cells. On the other hand, their cytoplasm does not always stain equally well with methylene blue, and the basophilia of the cytoplasm, therefore, is not as strong as with ordinary mammary gland cells, of which the basophilia of the cytoplasm and, hence, the content of ribose polynucleotides was found to be very strong in the present investigation. — As mentioned previously (p. 23), Caspersson & Santesson have found that the ribose polynucleotides content of the cytoplasm of a cell is particularly prominent in glandular cells producing protein. Hence it is understandable

that the basophilia of the cytoplasm of mammary gland cells is strong, but since it is weak in the »pale» cells, as observed, this supports the assumption that they are related to sweat gland cells. Hence the above-mentioned high cylindrical cells in this respect too may represent an intermediate form between the ordinary mammary gland cells and the »pale» cells, and in the present paper will be termed the »*intermediate epithelium*». On this basis it could be thought, further, that the

TABLE 12. — »PALE EPITHELIUM» IN CASES OF GYNECOMASTIA WITH AND WITHOUT »INTERMEDIATE EPITHELIUM»

	»Intermediate epithelium»		
	+	—	Total
»Pale epithelium» +	7	12	19
—»— —»— —	4	168	172
Total	11	180	191

»pale» and »intermediate» epithelium might represent *different kinds of secretion of the same cell type.* — In the present investigation a »pale» and »intermediate» epithelium were sometimes found in the same duct (Photo 24), where, without any clear demarcation, they passed over to one another. Some ducts were seen to contain both a »pale» and a normal mammary gland epithelium (Photos 21, 22), some an »intermediate» and a normal epithelium, and some even all three types (Photo 24). — In addition to the 7 preparations mentioned, the material contains 4 additional cases with an »intermediate epithelium»; hence, the number of preparations containing an »intermediate epithelium» in the present material totals 11.

As there were so many instances of one preparation containing both a »pale» and an »intermediate» epithelium, it was considered necessary to study whether this was a coincidence or whether these epithelial cell types were closely related. It was found, as is shown in Table 12, that a statistically significant *interdependence obtains between the »pale» and the »intermediate» epithelium* ($P_1 - P_2 = 57.3 \pm 15.3$ %).

and that they are therefore more closely related mutually than to the normal mammary gland epithelium. — On the basis of the above, it seemed justifiable to treat the gynecomastia preparations containing one of the two, either the »pale» or the »intermediate» epithelium, as a single group. Doing this, it was found that their histological properties differed from the corresponding properties of the entire material (Table 11) on practically one point only, that in the preparations of the previous group the majority of the epithelial cells in most cases (14 out of 23) consisted of cylindrical cells, in the total material again of cuboidal cells (the difference proved similar when the histological properties of the preparations containing the »pale» epithelium only or those containing the »intermediate» epithelium only were compared with the preparations of the total material). In addition, it was found (Table 13) that the difference was so great ($P_1 - P_2 = 39.6 \pm 10.7\ \%$) that it could not be attributed to a coincidence, but was statistically significant. — It therefore seems that *the »pale epithelium», the »intermediate epithelium», and the cylindrical epithelium might have a closer mutual interdependence than they have to the other mammary gland epithelium*, which constitutes the main part of the gynecomastia epithelium. — It can be mentioned that F r a n z a s is of the same opinion regarding female Mastopathia cystica and, hence, employs the general denomination »high epithelium».

It could be assumed that the secretory capacity of the glandular epithelium differs in those gynecomastia tissues whose biopsy specimens contain a »high epithelium» (i.e., the preparations have either a »pale» or »intermediate» epithelium or a mostly cylindrical epithelium) from that of the tissues in which the main part of the epithelium is low (i.e. cuboidal or flat). A study of this point showed, however, that there was no essential difference in this respect between the said groups, but that evidence of secretion was found in them relatively equally often.

Many investigators have considered the »pale epithelium» as an involution phenomenon. — In the present investigation it could be seen that in the different age groups the incidence

of preparations with a cylindrical epithelium in the majority and of those preparations with either a »pale» or an »intermediate» epithelium was the same. The age of the patient, therefore, appears to be of no importance in this respect. — Further, a study was made of whether a »high» epithelium

TABLE 13. — CYLINDRICAL EPITHELIUM IN GYNECOMASTIA PREPARATIONS WITH AND WITHOUT »PALE» OR »INTERMEDIATE» EPITHELIUM

	»Pale» or »intermediate» epithelium		
	+	—	Total
Cylindrical epithelium + ...	14	36	50
—»— —»— —	9	132	141
Total	23	168	191

TABLE 14. — PROPORTION OF »HIGH» (i.e., CYLINDRICAL, »PALE» AND »INTERMEDIATE») AND »LOW» (i.e., CUBOIDAL AND FLAT) EPITHELIUM IN FRESH AND OLD CASES OF GYNECOMASTIA

Duration of anamnesis	Number of cases with »pale» or »intermediate» or generally cylindrical epithelium	Number of cases with generally cuboidal or flat epithelium	Total
$\leqq$ 3 months	16	53	69
$>$ 3 months, $<$ 1 year	10	16	26
$\geqq$ 1 year	23	32	55
unknown	12	29	41
Total	61	130	191

was more frequent in old cases of gynecomastia, with an anamnesis of $\geqq$ 1 year, than in fresh ones, with an anamnesis $\leqq$ 3 months. It was found, as shown in Table 14, that the »high» epithelium is present considerably more often in the group of old cases of gynecomastia than in that of the fresh, and that this difference is so distinct ($P_1—P_2 = 19 \pm 8.2\ \%$) that it can very probably be considered statistically significant. It therefore seems possible that the »high» epithelium might represent some sort of involution phenomenon in gynecomastia.

As the male mammary gland is a rudimentary organ and does not, even when enlarged, nearly correspond to the female mammary, gynecomastia is evidently not maintained by the normal »female» mammary stimuli. Thus it seems natural that gynecomastia might conceal a constant tendency to involution. Since v. Gusnar, in addition, found that the »pale» and the »intermediate» epithelium was fairly frequently present in the normal mammary gland of the male, but that they were seldom seen in gynecomastia, it seems quite credible that *the »pale» and »intermediate» epithelium might represent an involution phenomenon.* On the basis of the above it could be assumed that *the cylindrical epithelium also might be an involution phenomenon.* In that case the course of the involution would be approximately as follows: cuboidal epithelium —> cylindrical epithelium —> »intermediate epithelium» —> »pale epithelium». In the involution of a cylindrical mammary gland cell the ribose polynucleotides, therefore, would gradually disappear from its cytoplasm, which would suggest the inactivation, possibly the degeneration, of this cell.

On the basis of the present investigation v. Numers' and Karsner's opinion can be endorsed — that the epithelial cells in gynecomastia are generally cuboidal and sometimes cylindrical — as can Moskowicz's and Semb's opinion — that the epithelium in gynecomastia is generally 2-layered. — The fact that some investigators in the former respect have been of the opinion that the epithelial cells in gynecomastia are generally cylindrical may be due to their material being too small to give an over-all picture. The fact again that e.g. Karsner and Erdheim considered the epithelium in gynecomastia as consisting generally of 3 or more layers may be because, in judging this point, they have also considered the proliferation of the epithelium.

As regards the »pale» and »intermediate» epithelium, it can be established that the latter apparently has not been described as occurring in the male mammary gland by anybody other than v. Gusnar and v. Numers, and of them, the former only has considered it in connection with the »pale epithelium». The present investigation probably can be con-

sidered as having proved their mutual relationship, but in addition the mutual relationship between them and the cylindrical epithelium of the mammary gland is taken as probably proved. — Furthermore it has been possible to advance support for the assumption that the »pale», the »intermediate» and the cylindrical epithelium in gynecomastia represent an involution phenomenon, a theory no one else has been found to advance previously with regard to gynecomastia. According to this, *the involution of the glandular cell in gynecomastia might begin with a morphological change of the cell, and this would then be accompanied by the disappearance of ribose polynucleotides from the cellular cytoplasm.*

2. Acini and lobuli in gynecomastia

Erdheim and v. Gusnar sometimes observed acini and lobular structure in the normal mammary glands of the male. Moszkowicz, Erdheim, Semb and v. Numers found both in their gynecomastia cases. Bertels sometimes found lobuli in his cases of gynecomastia but makes no mention of generally finding acini in them. Karsner reported that his cases of gynecomastia revealed no lobuli and apparently no acini either, although he did not wish to deny absolutely that the latter might be present in gynecomastia. Geschickter pointed out that no lobuli were present in his cases of gynecomastia; regarding acini he made no statement. Stieda found neither of the two in his cases.

In the present Finnish material lobular structure was observed in 25 cases (Table 11) or in one-eighth of all the cases of gynecomastia (Photos 11, 12). — As the epithelium in the glandular ducts of these lobuli was often found to be 1-layered while generally the glandular epithelium in the gynecomastia cases of the material was 2-layered, as is shown by Table 11, such glandular elements of the lobuli must probably be considered as acini. As the two-layered glandular epithelium too in gynecomastia possesses secretory capacity, as will be reported in detail later, it is obvious that no further characteristics, in addition to the above two, can be required of the acini.

Hence, it would seem, on the basis of most of the other investigations as well as the present, that *acini and lobuli, to some extent, are present in gynecomastia* and sometimes even in the normal male mammary gland.

3. Occurrence of secretion in gynecomastia

E.g. Erdheim and Forssell have found microscopically in both the small and the larger ducts of the mammary glands of newborn male infants plenty of eosinophilic cell-free secretion and, in this, often an abundance of desquamated epithelial cells. According to Erdheim's observations the epithelium was 2-layered in the small ducts also, according to Forssell generally 2- or multilayered, sometimes 1-layered. At a later age eosinophilic secretion was visible seldom only, according to Erdheim, in the normal male mammary gland. v. Gusnar, on the other hand, came to the conclusion that the majority of the cells in the normal mammary gland of the male produces an eosinophilic, mostly homogenous secretion, often in fairly considerable quantities. He also found a distinct apocrine type of secretion in his cases.

Moszkowicz, Erdheim, Semb, v. Numers, Geschickter and Karsner found secretion in the glandular ducts of gynecomastia; this Erdheim found to be cell-free, v. Numers cell-free, eosinophilic, sometimes containing desquamated cells, and Karsner in the majority of cases acidophilic, cell-free, or acidophilic, granular, less frequently basophilic, granular. Stieda found desquamated epithelial cells in the ducts of one of his gynecomastia cases but no further secretion, but Menville maintained that the mammary gland is a holocrine gland and therefore that only the desquamated epithelial cells — which he found fairly often in the ducts — represented the mammary gland secretions, and that the tubuli in the mammary gland, producing cell-free secretion, which he also observed in his preparations, were sweat glands. — Moszkowicz found apocrine secretion in the cells of the glandular ducts in his gynecomastia cases, both in the small and large ducts. Erdheim

also observed such secretion in some of his gynecomastia cases, as did v. Numers.

In the present investigation cell-free secretion was often found in the lumen of the ducts, in some 70 % of the preparations (Photos 10, 12, 25, 26, 27). In nearly half these cases desquamated epithelial cells, in addition to cell-free secretion, were found in the ducts (Photos 10, 26, 27), and in some gynecomastia preparations desquamated epithelial cells only and no cell-free secretion were seen in the ducts. — The cell-free secretion found has mostly been acidophilic, but basophilic secretion has also been seen.

Distinct apocrine secretion of the epithelial cells of the inner layer was found in the medium-sized ducts of some of the preparations of the material; the epithelium was generally 2-laiyered in these cases (Photos 25, 27).

The result arrived at in the present investigation, therefore, is that *in gynecomastia the glandular epithelial cells possess secretory capacity, — not only those of the small, acinus-like ducts but also those of the larger, in which the epithelium is 2-layered.* — The secretion mechanism is probably, in part at least, merocrine, as cell-free secretion is found remarkably often, but signs of apocrine secretion have also been observed, although fairly seldom.

The above results are in keeping with the observations of most investigators and apparently correspond also to conditions obtaining in the normal male mammary gland. Menville's conception only is obviously limited, as he assumed that the mammary gland in general has a purely holocrine type of secretion.

4. Type and significance of connective tissue in gynegomastia

Andrews & Kampmeier, Erdheim and v. Gusnar, who studied the normal mammary glands of men of all ages, and Karsner, who studied those of young men, found that their main part consisted of connective tissue. According to the observations of the last three of the investigators mentioned, the connective tissue of the normal male mammary

glands was similar throughout, and no looser around the glandular ducts than elsewhere. Andrews & Kampmeier, again, found periductal connective tissue also, fairly sharply distinguished from the dense connective tissue stroma; the periductal tissue consisted of more weakly stained fibrils and contained a larger number of nuclei.

In gynecomastia also investigators, such as Stieda, Bertels, Consten, Andrews & Kampmeier, Erdheim, v. Gusnar, Semb, Menville and Karsner, found the connective tissue predominating over the other types of tissue, most of it »fibrous», fairly dense. But, in addition, the above investigators and Moszkowicz, v. Numers and Geschickter have also found, some in a few, some in fairly numerous cases of gynecomastia, periductal, looser connective tissue, richer in nuclei, which Moszkowicz termed »mantle connective tissue» (Mantelbindegewebe). Andrews & Kampmeier and Erdheim found that the »mantle connective tissue» stained more weakly than the fibrous connective tissue, Semb that it stained with haematoxylin. Andrews & Kampmeier said that the »mantle connective tissue» was »greatly reminiscent of growing tissue and it had often been mistakenly considered as proliferating fibrous tissue». Moszkowicz, v. Gusnar, Semb and Menville again considered it as young connective tissue; Semb pointed out further that the fibrous connective tissue too in gynecomastia is fairly young as neither of the types is present in the normal male mammary gland in as large quantities as in gynecomastia, while »mantle connective tissue» was younger still. — Menville was able to establish that »mantle connective tissue» was mainly present in fresh cases of gynecomastia. — It is observed, therefore, that all investigators have been unanimous in maintaining that both the normal male mammary gland and gynecomastia consist mainly of connective tissue. In the normal male mammary gland this seems, for the most part at least, to be uniform and fibrous, whereas most of the investigators have found that loose periductal »mantle connective tissue» also occurs in gynecomastia in addition to the principal fibrous connective tissue;

the majority of these investigators, however, have not explained the nature and significance of the »mantle connective tissue».

From the present Finnish material it was also possible to ascertain that *the main element of gynecomastia is connective tissue, which for the greatest part is fibrous.* This fibrous connective tissue has more often, in some 60 %, been poor than rich in cells, as can be seen from Table 11. Fairly often, in some 70 % of the cases, it has been found to reveal hyaline degeneration which has more frequently been abundant in quantity than scanty (Table 11). — Due to Semb's assertion that the connective tissue in gynecomastia grows more hyaline and sclerotic with its age, a study of this has been made with the present material. It was found, as shown in Table 15, that old cases of gynecomastia, with an anamnesis of $\geqq$ 1 year, revealed hyaline degeneration relatively equally often as the fresh ones, with an anamnesis $\leqq$ 3 months. Furthermore, it can be seen from Table 11 that hyaline degeneration is found in all age classes in roughly the same proportions. — Hence, it was not possible to establish, on the basis of the present material, the laws governing it in gynecomastia, but only to conclude that *hyaline degeneration is such a general phenomenon in gynecomastia that it must probably be considered an essential feature of its microscopic picture, which is not,* contrary to Semb's assumption, *dependent on the age of the mammary gland enlargement, nor does it seem to depend on the age of the patient.* — Table 11 shows further that the absence or scantiness of »mantle connective tissue» in gynecomastia does not depend on the age of the patient, as it is found relatively equally often in all the age groups. Against this, it was established, as is shown in Table 16, that *in the old gynecomastia enlargements the connective tissue is more dense than in the fresh,* which again contain plenty of »mantle connective tissue». In addition, this difference is so great that it is statistically significant ($P_1 - P_2 = 24.7 \pm 8$ %) and therefore corroborates the observation by Menville and the assumption by Semb that connective tissue in gynecomastia grows more sclerotic the older the enlargement.

In the present material periductal loose »mantle connective tissue» was found in over two-thirds of the cases, i.e. relatively often (Photos 10, 13, 14). An investigation into the factors on which its presence might be dependent revealed — as was conversely stated above and as Menville has also found — that *»mantle connective tissue» is mainly present in fresh cases of gynecomastia* (Table 16) and that this finding, by

TABLE 15. — HYALINISATION DEGREE OF CONNECTIVE TISSUE STROMA IN FRESH AND OLD CASES OF GYNECOMASTIA

Degree of hyalinisation	Duration of anamnesis	
	≤ 3 months	≥ 1 year
Connective tissue not at all hyalinised	20	19
—»— —»— slightly —»—	8	11
—»— —»— partly —»—	14	5
—»— —»— abundantly —»—	12	7
—»— —»— almost entirely hyalinised	10	8
—»— —»— throughout —»—	2	4
Total	**66**	**54**

TABLE 16. — PRESENCE OF »MANTLE CONNECTIVE TISSUE» IN GYNECOMASTIA COMPARED WITH THE DURATION OF THE ANAMNESIS

»Mantle connective tissue»	Duration of anamnesis	
	≤ 3 months	≥ 1 year
— (none)	9	20
± (scant)		8
+ (fairly abundant)	30	18
++ (abundant)	26	6
Total	**65**	**52**

binomial distribution, is statistically significant. — Haematoxylin-eosin staining showed that »mantle connective tissue» stains with haematoxylin and is therefore basophilic, while fibrous stroma stains with eosin and is thus acidophilic (Table 17).

The so-called metachromasia phenomenon in gynecomastia has also been studied in the light of the present material, and the results are given in Table 17. It is seen that *free meta-*

TABLE 17. — STAINABILITY OF CONNECTIVE TISSUE BY HAEMATOXYLIN, PRESENCE OF FREE METACHROMATIC SUBSTANCE AND MAST CELLS IN THE CONNECTIVE TISSUE

	»Mantle connective tissue«	
	— or ±	+ or + +
Connective tissue (»mantle connective tissue«):		
not stained by haematoxylin	21	—
stained » —»—	—	34
Free metachromatic substance in the »mantle connective tissue« or in the neighbourhood of glandular ducts:	**20**	**36**
none	5	—
scant	11	1
moderate	3	5
fairly abundant	1	17
abundant	—	13
Mast cells in the »mantle connective tissue« or in the surroundings of glandular ducts:	**20**	**36**
(none)	—	—
scant	7	1
moderate	8	6
fairly abundant	3	20
abundant	2	9
Mast cells:		
also elsewhere in the connective tissue	4	12
nowhere else » » —»— —»—	16	34

chromatic substance and mast cells are present practically only in the »mantle connective tissue«; application of the equations of binomial distribution showed that the phenomenon was statistically significant and therefore cannot be the result of mere coincidence ($P_1 - P_2 = 78.3 \pm 7.9$ %). — As, according to L i s o n and S y l v é n, free metachromatic substance means high molecular ester sulphuric acids and the mast cells contain heparine, and these, according to S y l v é n, are found in great quantities and constantly only in biological conditions where new formation of connective tissue is in progress, it is obvious that *»mantle connective tissue« is fresh, newly formed connective tissue.*

The present investigation therefore corroborates Menville's, Moszkowicz's, v. Gusnar's and Semb's opinion that »mantle connective tissue» indicates young, newly formed connective tissue, fibrous stroma again older, and that the new formation of connective tissue, hence, takes place around the glandular ducts only. — From this it would also appear natural that »mantle connective tissue», as found by Andrews & Kampmeier, Erdheim, v. Gusnar and Karsner, is not present in the normal male mammary gland, at least not in any considerable quantity, as it is an essential factor in the enlargement of the mammary gland.

Obviously the fact that new formation of connective tissue in gynecomastia takes place immediately around the glandular ducts also means that in gynecomastia the glandular ducts too grow. In the present investigation as well it has been possible to establish microscopically that the glandular ducts on each side extend to the periphery of the gynecomastia enlargement, to where the mammary gland, thus, has expanded. In addition, proliferation of the epithelium of the glandular ducts could be seen microscopically in nearly half the preparations. Hence, *gynecomastia in fact represents fibroepithelial hyperplasia of the mammary gland*, as emphasised particularly by Semb.

5. Cysts and their origination mechanism in gynecomastia

In investigating normal male mammary glands v. Gusnar has often observed cystic dilatation of the glandular ducts in preparations. Consten found that the majority of his cases of »diffuse fibromatosis» revealed cysts. Erdheim found that in gynecomastia both the small and medium-sized, but often also the large ducts had expanded »almost cystically». Semb again, in his cases of male »fibroadenomatosis» found that some ducts only had dilated into a roundish shape, and »possibly a few round acini», but no distinct cysts such as are present in female »Maladie cystique». Menville, on the other hand, often found duct dilatation in his gynecomastia cases, as did v. Numers and Karsner. — As regards

the general origination mechanism of the cyst-like dilatations found in the mammary gland, Consten considers the cysts to be produced by exaggerated growth of the connective tissue, which dilates the acini into cysts. Erdheim again was of the opinion that the duct dilatations were connected with the presence of the secretion, and this opinion seems to have been shared by v. Gusnar and Karsner. Bertels attributed the cyst-like dilatations to the newly formed connective tissue constricting the ducts, when the retention of the secret-

TABLE 18. — SECRETION IN THE LUMEN OF THE GLANDULAR DUCTS IN CASES OF GYNECOMASTIA WITH AND WITHOUT CYSTS

Secretion	Cysts		
	+	—	total
+	129	9	138
—	36	17	53
Total	165	26	191

TABLE 19. — SECRETION OR EPITHELIAL DESQUAMATION IN THE LUMEN OF THE GLANDULAR DUCTS IN CASES OF GYNECOMASTIA WITH AND WITHOUT CYSTS

Secretion or desquamation	Cysts		
	+	—	total
+	141	12	153
—	24	14	38
Total	165	26	191

ion dilated the acini, and he gave as the reason why no cysts were found in his cases of male »mastitis chron. cystica» that males have no acini. Semb was of the opinion that cystically dilated ducts cannot be termed cysts proper but only dilated acini, but he assumed, however, that both these dilatations originate in the same way, viz. from the retention of the secretion induced by newly formed connective tissue.

Cyst-like dilatations have often been found in the present material, particularly in medium-sized but also in small and

large ducts — according to Table 11 in 86 % of the preparations. In these dilated ducts the epithelium is generally 2-layered, but a 1-layered epithelium has also been seen (Photos 25, 26, 27). As, however, a 1-layered glandular epithelium is relatively rare, and the cysts covered by the 2-layered epithelium are also often very beautiful and of typical shape, and as there seems to be no difference in principle yet in the secretory capacity of the 1- and 2-layered epithelium, as mentioned on page 44, the cyst-like dilatations covered by any of these epithelia have been considered as identical formations. This in spite of the conclusion that the small glandular ducts, with a 1-layered epithelium, are taken to be acini in the present investigation, as described on p. 44.

In reviewing the origination mechanism of the cysts found in the gynecomastia cases of the present material it was found that, in the preparations with cysts, acidophilic or basophilic cell-free secretion is present in the glandular ducts, particularly in those cystically dilated, more often than in the preparations in which no cysts were observed. This difference is so considerable, as can be seen from Table 18, that it cannot be assumed as coincidental but is statistically significiant ($P_1 - P_2 = 43.6 \pm 9.9$ %). Hence, it could be established with certainty that *an interdependence obtains between the cysts and the secretion in the gynecomastia* cases of the present material. — Taking into consideration the presence of both cell-free secretion and of desquamated epithelial cells in the lumen of the glandular ducts, the same result as is given in Table 19 was attained ($P_1 - P_2 = 39.3 \pm 10.2$ %). — Proliferation of glandular epithelium has been observed microscopically relatively as often in the preparations with cysts (76 out of 165) as in those with no cysts (11 out of 26), and hence it does not, at least directly, seem able to cause the cysts. However, it must be borne in mind that in the preparations where the cysts are most numerous and largest the cystic epithelium in particular is generally flat; this again may be a secondary phenomenon resulting from intracystic pressure, and it may be possible that in the initial stages of the origination of the cyst the epithelium may have been higher, and

even proliferating. — Table 20, again, shows that *in gynecomastia preparations with cysts, »mantle connective tissue» is present relatively more often than in those without cysts.* It was also found that the difference is so great that statistically it is very probably an expression of true interdependence ($P_1 - P_2 = 22.7 \pm 10.4$ %). — On the other hand it is known (p. 49) that »mantle connective tissue» is present

TABLE 20. — »MANTLE CONNECTIVE TISSUE» IN CASES OF GYNECOMASTIA WITH AND WITHOUT CYSTS

»Mantle connective tissue»	Cysts +	Cysts —	total
+ or ++	120	13	133
+ or ±	45	13	58
Total	165	26	**191**

TABLE 21. — PRESENCE OF CYSTS IN FRESH AND OLD CASES OF GYNECOMASTIA

Cysts	Duration of anamnesis: 3 months	3 months, 1 year	1 year	unknown	total
+	64	24	45	32	165
—	5	2	10	9	26
Total	69	26	55	41	**191**

mainly in fresh cases of gynecomastia; it can be seen from Table 21 that cysts are relatively more frequent in fresh cases of gynecomastia (anamnesis $\leq$ 3 months) than in cases with an anamnesis of $\geq$ 1 year, but also that the difference is so small that it may be coincidental in origin ($P_1 - P_2 - 11 \pm 6.1$ %). — However, it can probably be thought that the growth process on which gynecomastia is based, fibro-epithelial hyperplasia, with which the presence of »mantle connective tissue» is connected, might tend to block the lumen of the glandular ducts and thus obstruct the secretory outlet; indeed, it seems improbable that it might force the duct walls out-

ward. In such conditions continued secretion would increase pressure within the duct and might cause its dilatation. — This, as mentioned above, was also S e m b's conception of the origination mechanism of cysts in the mammary gland, and to some extent also that of B e r t e l s. — As regards the incidence of cyst-like duct dilatations, again, the majority of investigators have arrived at the result attained in the present investigation also, viz. that they are often seen in gynecomastia; v. G u s n a r found them fairly common in the normal male mammary gland also.

6. Sweat glands in gynecomastia

v. G u s n a r found in the normal male mammary gland both eccrine and, from the age of puberty onwards, apocrine sweat glands, and often also intermediate forms between one of these two and the mammary gland epithelium. Further, he found that the number of apocrine sweat glands decreases at more advanced ages. K a r s n e r also observed apocrine sweat glands in the normal male mammary gland. — M e n v i l l e reported having seen ordinary sweat glands sometimes in gynecomastia, and G e s c h i c k t e r mentioned that hypertrophy of the subcutaneous sweat glands may be connected with gynecomastia. S e m b in his cases of gynecomastia sometimes saw both sweat glands with a »pale» epithelium and sweat glands difficult to distinguish from ordinary mammary gland tubules. K a r s n e r also found ordinary sweat glands in his cases of gynecomastia, and noticed apocrine sweat glands in a good tenth of his cases; he could establish no distinct correlation between the condition of the apocrine sweat glands and the proliferative or inflammatory changes of the adjacent mammary gland tissue.

Apocrine sweat glands were found in 21 cases in the present investigation, i.e. in approx. one-tenth of the cases. They were situated in the subcutaneous tissue, and were fairly regular in shape; the cells were in one layer, the nuclei in the basal part of the cell, and generally small; the cytoplasm stained poorly with haematoxylin-eosin and haematoxylin-v. Gieson

methods and seemed typically »pale» (Photo 28). The different phases of apocrine secretion could be seen in these glands.

The cases with apocrine sweat glands occurred in all age groups, except for the 30—39-year group, as can be seen from Table 11, with over 50 % in patients of 50 or older. — On the other hand, apocrine sweat glands were found more often in fresh (anamnesis $\leq$ 3 months) than in old (anamnesis $\geq$ 1 year) gynecomastia enlargements, in contrast to the occurrence of the »pale» or »intermediate» epithelium (Table 22).

Ordinary eccrine sweat glands were observed in the present material less frequently than the apocrine — in five cases only. They too were situated in subcutaneous tissue; their epithelium bore a close resemblance to that of the ordinary mammary gland ductule, but was slightly lower and more regular; the secretion contained no desquamated cells.

According to the present investigation, therefore, the amount of apocrine sweat glands does not decrease in gynecomastia at an advanced age, as v. Gusnar ascertained of normal male mammary gland cases. This may be the very reason for the difference. — Regarding the fact that apocrine sweat glands were found in the present material more frequently in fresh than old gynecomastia enlargements no particular conclusion can be drawn, due to the relatively small number of cases.

TABLE 22. — »PALE EPITHELIUM», »INTERMEDIATE EPITHELIUM» AND APOCRINE SWEAT GLANDS IN GYNECOMASTIA GROUPS OF DIFFERENT DURATION

Duration of anamnesis	»Pale» or »intermediate» epithelium +	Apocrine sweat glands +
< 3 months	6	10
> 1 year	10	2
> 3 months < 1 year	1	4
unknown	6	5
Total	23	21

7. "Inflammation cells" and their significance in gynecomastia

In the normal mammary gland of the male both Andrews & Kampmeier and v. Gusnar have often found small inflammation cell infiltrates, mainly in the environment of the ducts; the former reported that these cells were »leukocytes», v. Gusnar spoke of »round cells». According to Karsner, some lymphocytes are often present close to the ducts in the normal mammary gland of the male. — Andrews & Kampmeier, in their cases of »Mastitis chronica», often reported round cell infiltration around the ducts, though never particularly distinct. Menville, v. Numers, Geschickter and Karsner found round cells fairly often in their cases of gynecomastia, mainly in the periductal connective tissue, the last-mentioned often also reporting polymorphonuclear cells. Erdheim and Semb reported round cell infiltration only seldom in gynecomastia, and then as a rule in the periductal connective tissue. — As regards the significance of the inflammation cells in the normal and enlarged mammary of the male, Andrews & Kampmeier were strictly of the opinion that a real inflammation was involved in both cases, though they did not explain how the normal male mammary gland could be regularly inflamed. Menville was of the opinion that an inflammation no doubt had been present in some cases of gynecomastia. Against this, all the other investigators mentioned above, and Moszkowicz, considered that the infiltrates observed were practically never large enough to be considered as signs of an inflammation proper, but that they were an expression of intensified vascularisation connected with the growth of the tissues or with resorption phenomena.

In all the gynecomastia preparations of the present material inflammation cell infiltrates were observed microscopically in the periductal connective tissue, and in some cases perivascular inflammation cell infiltration was found elsewhere in the stromal connective tissue. — Inflammation cell infiltration, in some 85 % of the cases was slight, inflammation cells were present in »fair amounts» in some 14 %

of the cases and »fairly abundant» in 1 % only (Photo 21). — These inflammation cells were generally mononuclear, with lymphocytes in the majority, some mast cells and a small amount of plasma cells. Polymorphonuclear cells were seen fairly seldom only.

As established previously (p. 50), the »mantle connective tissue» is young, newly formed, and constitutes the second main phenomenon of fibro-epithelial hyperplasia of the normal mammary gland of the male leading to gynecomastia. As it is in this tissue mainly that inflammation cell infiltrates are found, it is obvious that *they do not indicate inflammation but are an expression of the intensified blood circulation connected with the growth of the tissues. They are undoubtedly often also a reaction caused by the degenerating tissue.* This is supported by the fact that these infiltrates are generally small.

It can be stated that the observations made in the present investigation on the inflammation cells and their significance comply with the observations of most other investigators.

8. What is the patho-anatomical character of gynecomastia?

The historical introduction (p. 2) revealed that conceptions held by the different investigators regarding the patho-anatomical nature of gynecomastia have been fairly varying.

The present investigation has shown that gynecomastia is no growth proper (p. 33), nor is it an inflammation (p. 58). It was found that hyperplasia of connective tissue (p. 48) and of glandular epithelium (pp. 38, 51) are characteristic of it, and that other connected phenomena such as cysts and inflammation cell infiltrates are only consequences of these two fundamental phenomena (pp. 54, 58). In addition, gynecomastia comprises, as a degenerative phenomenon, the fairly frequently encountered hyalinisation of fibrous connective tissue, and the cysts can also be considered a degeneration phenomenon.

The present investigation finds, therefore, that *the patho-anatomical character of gynecomastia is fibro-epithelial hyperplasia of the mammary gland of the male, connected with which are the degenerative changes in the fibrous connective tissue.*

Certain investigators, e.g. Bertels, Semb, v. Numers and Sullivan & Munslow, have considered gynecomastia and female Mastopathia cystica similar patho-anatomical phenomena. — The original conception of Maladie cystique Reclus referred to a mammary gland disease with cysts discernible even macroscopically. But as pointed out by e.g. Semb, its basic nature was fibro-epithelial proliferation of the mammary gland; macroscopically observable cysts are often not present in the initial stage, but sometimes cysts visible microscopically, and sometimes not even that. Semb also often found hyaline degeneration of fibrous connective tissue in Mastopathia cystica.

An application of the above definition of Mastopathia cystica employed by Semb shows that the patho-anatomical nature of gynecomastia is the same: fibro-epithelial proliferation. — In addition, it was found in the present investigation that in gynecomastia it is just this fundamental phenomenon, fibro-epithelial hyperplasia, that probably accounts for the origination of cysts (p. 54). — This result was also arrived at by Semb regarding female Mastopathia cystica.

The consideration of gynecomastia as a patho-anatomical process similar to female Mastopathia cystica, therefore, is fully justified. But, on the other hand, differences exist between gynecomastia and female Mastopathia cystica. Firstly, the outward shape of a gynecomastia breast almost always differs from that of the female breast. Secondly, the microscopic picture of gynecomastia is also distinctly different from that of female Mastopathia cystica. The basic element in gynecomastia is connective tissue; lobular structure occurs rarely and, if present, is defective; in the female breast the case is almost the opposite. Accordingly cysts in female Mastopathia cystica have usually developed from the acini, in gynecomastia as a rule from glandular ducts (p. 52). —

Thirdly, gynecomastia originates from the male mammary gland, a rudimentary organ, growing in size, whereas female Mastopathia cystica originates in the degeneration of a normal female breast, capable of activity.

Although, therefore, as a patho-anatomical process gynecomastia is similar to female Mastopathia cystica, its patho-anatomical basis, however, is entirely different. From this point of view, there is every justification to regard it as a special pathological phenomenon and also to apply a special denomination to its occurence. As the name »gynecomastia« indicates that an enlargement of the male mammary gland resembling the female breast is in question, as this is a traditional appellation, and as it is fairly generally employed at present, it seems suitable.

Etiology of the tumours of the male breast

It has not been possible in the present investigation to make any striking observations regarding the etiology of carcinoma or sarcoma of the male breast, and so it is hardly necessary to discuss it at any greater length. However, it may be mentioned that, according to the investigations by Lacassagne, Suntzeff & al., Cramer & Horning and Huseby & al., the estrogens seem to bear some relation to the origination of mammary gland carcinoma both in female and male mice, according to Allaben & Owen, Auchincloss & Haagensen and Parsons & McCall to that of female mammary gland carcinoma, and according to Abramson & Warshawsky to that of male mammary gland carcinoma.

Certain points of view on the etiology of gynecomastia have emerged in the present investigation, and it was therefore considered justifiable to report in brief on corresponding observations recorded in the literature. — Four main etiological causes have been advanced in the literature for gynecomastia: hereditary factors (Gangitano), inflammation (Andrews & Kampmeier), trauma (Semb) and, the largest group, discussed at the greatest length, hormonal factors. Endocrine glands, a disease of which has been assumed to cause gynecomastia, are the testis (Stieda, Bailey, Moszkowicz, Prange, Rose, D'Arcy-Prendergast, Heidrich & al., Ross, Gilbert, Cairns, Hunt & Budd, Menville), the pituitary gland (Heidrich & al., Schachter, Staemmler, Roth, Haenel), corpus pineale (Oestreich & Slawyk), the adrenal cortex (Mathias, Simpson & Joll,

Edwards & al., Lawrence), and the thyroid gland (Menville, Strand). Some investigators have considered extragenital chorionepithelioma as the etiological factor in gynecomastia (Bonn & Evans, Hagn-Meincke), some again functional disorder of the liver (Paula, Glass & al., Klatskin & Rappaport, Klatskin & al.,). Some have paid attention to gynecomastia's occurring mainly at certain periods of age (Zappert, Bailey, Moszkowicz, v. Gusnar, Semb, Jung & Shafton, Nathanson) and from this drawn conclusions as to its etiology, and a few investigators have reported cases where gynecomastia appeared immediately after prostatectomy (Kondoléon, Oppenheimer, Andrews & Kampmeier). It has been possible to produce gynecomastia by estrogenic substances (Hoffman, Dunn, Moore & al., Slobozianu), but also by androgenic (Dunn, Slobozianu) and with a chemical substance not related to hormones (amphetamine sulphate, Tooley & Lack). Investigations have been made into the influence of the age and sexual development of the male on the excretion of androgens, estrogens and gonadotropin (Hamburger & Halvorsen, Oesting & Webster, Yolton & Rea), but the results are to some extent contradictory. In gynecomastia the excretion sometimes of estrogen, sometimes of gonadotropin has been found (Luft) to have increased. On the basis of animal experiments it would seem that both estrogenic and androgenic substances and desoxycorticosterone may cause an enlargement of the mammary glands of the experimental animals (Gardner & al., Anselmino & al., Burrows, Selye, van Heuverswyn & al., Eisen), and that the castration of a male mouse at birth may produce hyperplasia of the adrenal cortex and growth of the mammary glands (Woolley & al.)

I. SIGNIFICANCE OF HEREDITY IN THE DEVELOPMENT OF MALIGNANT TUMOURS IN THE MALE BREAST AND OF GYNECOMASTIA

Of 18 male patients with a malignant mammary gland tumour and of 89 gynecomastia patients from the present material it is known whether or not malignant tumours have occured in their families. It appeared that malignant tumours ran in the family of two men suffering from a malignant mammary gland tumour, i.e. in 11 %, and that with 25 of the gynecomastia patients, or 28 %, malignant tumours had occured in the family. However, the difference between these percentages is so small that, statistically it may be due to a coincidence, for $P_1-P_2=17\pm8.8$ %. In addition consideration must be paid to the fact that these figures are based on information supplied by the patients themselves, and the reliance that can be placed on them is very small. However, a conclusion that can be drawn from the figures reported is that, as malignant tumours are found more frequently in the families of patients with gynecomastia than of those with a malignant mammary gland tumour, *heredity probably is of little significance in the development of malignant tumours of the male breast.* The tendency of gynecomastia to develop into a malignant tumour, as will be shown later, is slight, and it cannot be considered a precancerous condition.

Of the relatives of the gynecomastia patients in the present material, three only are known to have had gynecomastia. It is not known, admittedly, how many of them did not have it, but the number of the confirmed cases is so small that it is doubtful *whether heredity is of any importance in the occurence of gynecomastia,* contrary to Gangitano's opinion.

II. SIGNIFICANCE OF MECHANICAL TRAUMA AND INFLAMMATION IN THE ETIOLOGY OF TUMOURS OF THE MALE BREAST

Of 20 male patients with malignant and 3 with benign mammary gland tumours and of 88 gynecomastia patients, from the present material, it is known whether or not the breast had been exposed to trauma prior to the appearence of gynecomastia in it. In the first two groups trauma was reported in one case only, in the gynecomastia group in 10 cases. In the majority of cases the trauma had occured a fairly long time previous to enlargement of the mammary gland and just on one occasion. — Bearing in mind how exposed the thorax is to mechanical trauma, the conclusion may be permitted that *trauma is of no essential causative significance to the diseases in question.* — However, the opposite has often been maintained, e.g. regarding carcinoma, by earlier investigators, and regarding gynecomastia by S e m b, but their point of view has generally been rejected in the literature recently.

The present investigation gave *a negative result as regards the significance of inflammation in the origination of gynecomastia,* as was reported on p. 58. It was also mentioned in the same connection that this has been the opinion of the majority of other investigators as well.

III. SIGNIFICANCE OF EARLIER DISEASES IN THE ETIOLOGY OF TUMOURS OF THE MALE BREAST

But few of the patients in the present material had suffered from diseases in the genitalia before the mammary gland tumour made its appearance: in two cases out of six investigated in the group of malignant tumours and in 4 cases out of 64 in the gynecomastia group. — Diseases of the prostate had been somewhat more frequent: in the group of malignant tumours, 3 cases out of 10, in the gynecomastia group, 16 cases out of 80 investigated. All these patients were of advanced age, the youngest 46, the oldest 78, the average age being 61; hence, they were in the »prostate age». — Of interest are the two cases in which gynecomastia had developed soon after prostatectomy (in one of the cases the operation was for prostatic carcinoma, in the other for prostatic hypertrophy). Obviously, however, gynecomastia following prostatectomy is a rare occurrence for, as prostatectomies are performed often and on aged men, and as these patients are usually closely followed-up, nodes appearing in their breast would no doubt be noticed in most cases and would be removed and examined. It also seems probable that a larger number of similar cases would have been found in the literature than the few that have been found as published (p. 62), if this phenomenon were relatively common. — It therefore seems that *diseases of the genitalia proper and the prostata or prostatectomy play at least no essential part in the etiology of male breast tumours.*

Of particular interest from the etiological point of view is the case of mammary gland carcinoma that developed in a gynecomastia; it will be dealt with in detail later in this paper. — Tumours occuring elsewhere than in the breast, and

goitre, were reported by the patients so seldom that they are obviously of no etiological importance in the origination of mammary gland tumours in the male, particularly as 13 tumour and 69 gynecomastia patients reported that they had not suffered from tumours anywhere else prior to the enlargement of the mammary gland setting in. In addition, 8 patients with malignant mammary gland tumours and 2 with benign mammary gland tumours, as well as 68 patients with gynecomastia, reported that they had not had goitre. — As diabetes is a result of hormonal disorder, inquiry into this point was also made with the patients, and of the 10 tumour and 71 gynecomastia patients that replied not one reported having diabetes.

IV. ETIOLOGICAL SIGNIFICANCE OF DISEASES AND SYMPTOMS FOUND IN THE MALE SIMULTANEOUSLY WITH A MAMMARY GLAND TUMOUR

It could be established that 5 out of 12 examined patients with a mammary gland tumour and 7 out of the 76 examined gynecomastia patients of the present material displayed some genital deficiency. This deficiency was generally slight, and the majority of the tumour patients and the predominant part of the gynecomastia patients, as far as is known, had normal genitals. — Only 3 patients suffering from malignant tumour and 6 gynecomastia patients were known to have had hydrocele, varicocele, or strictura urethrae. — On the basis of the present material it would seem, therefore, that *genital disorders discernible at physical examination play at least no considerable part in the appearance of mammary gland tumours of the male,* and the same result has been arrived at by many other investigators as well, e.g. Erdheim, Semb, v. Numers, Sullivan & Munslow, Nathanson and Karsner. Those published cases, again, citing a simultaneous testicular defect or tumour and gynecomastia, have generally been occasional only. — *The sexual life* of the patients of the present material *also seems to have been normal generally.* Six of the patients with a mammary gland tumour and 28 gynecomastia patients reported how often, on the average, they had sexual intercourse, and of them, only 1 tumour patient and 2 gynecomastia patients copulated seldom or not at all, the others generally twice a week and at least once a month. Only 2 of the 13 tumour patients and 3 of the 58 gynecomastia patients examined had lived several years in childless marriage, while the others examined either had

children or got them soon after the mammary gland enlargement was removed. Two of the 6 tumour patients and 6 of the 58 gynecomastia patients examined reported impotence, but with all of them it had been temporary, and all the patients, apart from one, were of advanced age. — The result, therefore, gives no indication of any distinct sexual abnormalities being the general cause of enlargements of the male breast.

Of interest is the observation that the *hair growth of gynecomastia patients has fairly frequently been feminine*, whereas, as far as is known, this has not been so in a single tumour patient. The gynecomastia patients in question, totalling 12 (or 39 %) of the examined in this respect, were of varying age: the youngest 14, the oldest 68, average age 35 years. The said symptom has fairly generally been assumed to indicate some difference from the ordinary male type in the hormonal equipment. P r a n g e, for instance, in his time, stated that e.g. hair growth of »eunuchoid type» was often connected with gynecomastia, suggesting inferiority of sexual determination. — However, the patients voices in the present material seem to have been normally masculine, for the voice of all the 6 mammary gland tumour patients and of 31 gynecomastia patients examined in this respect was normal, while one gynecomastia patient only had a feminine voice.

Fat patients were relatively more numerous in the tumour group than in the gynecomastia group of the present material (in the former, 9 out of 23, in the latter, 10 out of 70), thin patients relatively more numerous in the gynecomastia group (31 out of 70) than in the tumour group (5 out of 23). This may be explicable, in part at least, from the fact that the patients in the latter group were younger, and young men are relatively seldom fat.

Two of the patients of the present material had received stilbestrol just before the appearance of the gynecomastia. Taking into consideration that similar cases have been reported in the literature (e.g. M o o r e & al.) and that the general clinical experience is that during stilbestrol treatment the patients' breasts often grow in size and become tender, it can

probably be considered as certain that *substances similar to estrogens may induce gynecomastia.*

The interesting case of patient V.V.P. may be described here. At 34, he became ill with gynecomastia, first in the left and a couple of months later in the right breast, both of which were subjected to ectomy. After some twelve months the patient found that his left testicle, which had been larger than the right — the latter had become atrophied after mumps — had been further enlarged, and three years later he became impotent. After another year the left testicle was removed, and malignant seminoma was found in it. No hormonal analyses could be effected on the case in the absence of laboratory facilities. — Case reports published in the literature record patients with simultaneous testicular tumour and gynecomastia. In cases reported by Heidrich & al., Ross and Gilbert the tumour was testicular chorionepithelioma, and in the urine of the majority of the patients an increase in gonadotropin, with some in estrin also, was observed. In Hunt & Budd's case there was an interstitial cell tumour, and in this case too the gonadotropin in the urine had increased. — It seems that in these cases the change found in the hormonal equilibrium constituted the direct cause of gynecomastia; whether the testicular tumour was the cause of the hormonal changes or vice versa, is difficult to state with any certainty so far. The case of V.V.P. reveals a clinical similarity to the cited cases in the literature, and it may be possible that in this case too the *testicular tumour may in its initial stage have produced gynecomastia*, or the two may have arisen from some other, identical factor.

Acromegaly, goitre, cirrhosis or other liver disorders, hydronephrosis, simultaneous malignant or benign tumours elsewhere in the organism, diseases of the blood circulation, psychic and other nervous disorders and infectious or parasitic disease of the intestines, because of their infrequent occurrence, do not seem to have any etiological significance in the origination of male mammary gland tumours according to the present material.

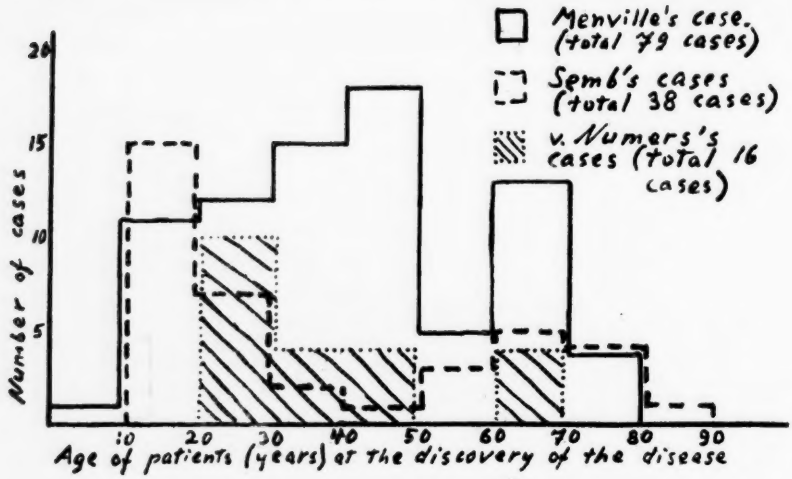

DIAGRAM 1. — NUMBER OF GYNECOMASTIA CASES BY AGE GROUPS IN MENVILLE's, SEMB's AND v. NUMERS's MATERIALS

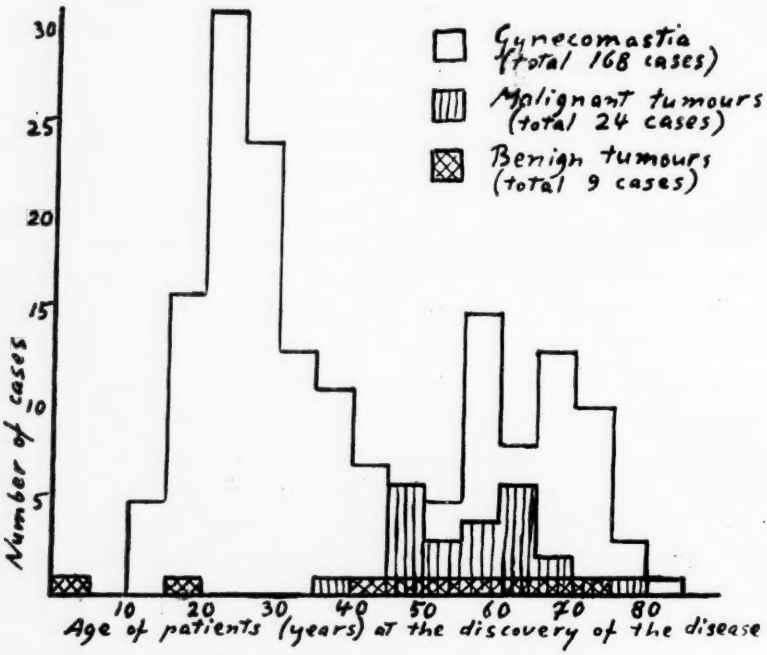

DIAGRAM 2. — NUMBER OF PATIENTS IN THE PRESENT MATERIAL, BY AGE GROUPS

Some investigators have found gynecomastia in their materials mainly at certain age periods, some at the age of puberty, some in the course of early old age, some during youth and in old age. — Diagram 1 shows Menville's Semb's and v. Numers's gynecomastia materials by age groups. It can be seen that all three diagrams reveal a mutual resemblance in that they display two distinct rises, a higher one in younger, a lower in the older age groups. — Diagram 2 shows the distribution of both the tumour and gynecomastia cases of the present material by age groups. It also shows that the gynecomastia picture displays two principal rises, of which the one coinciding with the younger age groups is distinctly higher. In addition, it can be seen that the rise for the older age groups coincides for a considerable part with the picture for malignant tumours. The highest point comes between the 20th and 30th year of age; the rise for the older age groups is more even, with a high point between 55 and 75. — The high points of the present material correspond with those of v. Numers's material, and also to those of Semb's material, fairly well; only in the latter the high point comes earlier, between the 10th and 20th year of age. The first rise in Menville's material differs more distinctly from the others: the rise develops fairly evenly from the 10th to the 50th year of age, with a high point between 40 and 50. — All these four materials are well comparable, for they have all been collected from a patho-anatomical laboratory and hence are treated broadly on the same basis. Since, in their main features, they give the same results for distribution into age groups, and as the present Finnish material is considerably larger than the others, it may be justifiable to assume that, of these four materials, the Finnish best corresponds to real conditions. — It can therefore probably be considered as certain that *gynecomastia occurs primarily in the age of puberty and that of the fullest sexual maturity, and secondly in praesenium and senium.*

V. HAS GYNECOMASTIA AN ETIOLOGICAL SIGNIFICANCE IN THE OCCURRENCE OF MAMMARY GLAND CARCINOMA IN THE MALE?

Certain sporadic cases have been reported in the literature where mammary gland carcinoma obviously has developed in gynecomastia. Such reports have been published by Berns, Peachell, de la Villeon, Woodham and Moriarty. In de la Villeon's case the gynecomastia had appeared soon after prostatectomy, in Woodham's case in a patient on whom bilateral orchidectomy had been performed earlier, and the patient described by Moriarty was a real hermaphrodite. — In addition, some investigators, in their extensive series of male mammary gland enlargements, have devoted attention to the question of whether gynecomastia might be a factor predisposing to malignant tumour. Among them, Andrews & Kampmeier and Semb arrived at a negative result. Of Gilbert's series of 47 cases of male mammary gland carcinoma 9 had gynecomastia as well, and among Geschickter's 30 cases 3. However, in Geschickter's series of 108 gynecomastia cases no malignant degeneration was observable in follow-up examinations, and the same applies to Menville's series of 88 gynecomastia cases. Gilbert and Geschickter were of the opinion that there might be some kind of interdependence between gynecomastia and male mammary gland carcinoma. It may be mentioned, further, that out of 12 patients with mammary gland carcinoma in Charache's material, one had gynecomastia also, and out of v. Nanay's 10 similar cases one had had gynecomastia in his youth.

In the present Finnish material only one of the patients with mammary gland carcinoma had gynecomastia of old.

At about 17 years of age both the patient's breasts had grown in size and continued to remain unchanged as formations in which enlargements of the size of half a fist, of glandular consistency, could be distinctly palpated. At 57, a hard lump the size of the end of a thumb appeared in the right breast, and on operation it was found to be Carcinoma solidum alveolare. — Of the gynecomastia patients of the present material, 20 had an anamnesis of $\geq$ 3 years at the moment of operation, 12 of them $\geq$ 5 years. No malignant degeneration could be observed in these cases. The present Finnish material would appear to show therefore, that *gynecomastia does not promote the development of mammary gland carcinoma in the male.* — As a reservation, however, it should be borne in mind that in some series *in the literature relatively and numerically more numerous cases of gynecomastia resulting in mammary gland carcinoma have been reported than in the present material.*

Clinical picture of tumours of the male breast

The method applied in the following is, generally, that representative publications in literature have been reported on in tabular form, and, to facilitate comparison, the corresponding figures of the present Finnish material have been inserted in the same tables.

TABLE 23. — AGE OF MEN SUFFERING FROM CARCINOMA OF THE BREAST AT THE DISCOVERY OF THE DISEASE, ACCORDING TO SOME INVESTIGATORS

	Number of cases	Age of patients (years) youngest	average	oldest
Wainwright	325	23	54.2	
Gilbert	47	31	54.4	83
Neal	50	30	57.7	89
Sachs	194	12	57.2	86
Present material	**22**	**39**	**56.8**	**76**

I. AGE OF THE PATIENTS

Table 23 shows the average age of the patients at the discovery of the disease in the materials of carcinoma of the male breast, and the ages of the youngest and oldest patient. The table shows that in the materials from the literature the average age varied from 54.2 to 57.7 years, and that in the present material it is 56.8 years, or within the same limits as the others. — It may be mentioned that the youngest male patient with mammary gland carcinoma found in the literature was the case reported by Blodgett, a 12-year old boy, while the oldest case was a man of 93, reported by Charache. In the present Finnish material the youngest carcinoma patient was 39, the oldest 76.

Information in the literature on the age of male patients with mammary gland sarcoma indicates that their average age has been distinctly lower than that of carcinoma patients. For instance, in Finsterer's material (11 cases) it was 47.2 years, in Mitterstiller's (35 cases) 42.8, and in Neal's material (9 cases) 39.8 years. The present Finnish material includes only 2 sarcoma patients; one of them, at the discovery of the disease, was 45, the other 69.

Diagram 2 shows the age of the tumour and gynecomastia patients of the present material at the discovery of the disease. It can be seen, e.g., that benign tumours have been found in patients of different ages, the older age groups being slightly in the majority.

The age of gynecomastia patients was reviewed on p. 71.

II. DURATION OF DISEASE PRIOR TO ECTOMY IN MALE PATIENTS SUFFERING FROM MAMMARY GLAND ENLARGEMENT

Formerly male patients with mammary gland carcinoma sought treatment at a fairly late stage of the disease. This is clearly seen in Table 24, which shows the percentage of patients seeking treatment within a year of the appearance of the

TABLE 24. — DURATION OF THE DISEASE PRIOR TO OPERATION WITH MEN SUFFERING FROM MAMMARY GLAND CARCINOMA, ACCORDING TO DIFFERENT INVESTIGATORS

	Total material	Duration of disease < 1 year	
		number	%
Williams	96	22	23
Wainwright	342	161	47
Schreiner	15	6	40
Gilbert	47	26	55
Neal	27	18	67
Sachs	174	106	61
Geschickter	30	18	60
Kappelgaard	50	32	64
Present material	**20**	**10**	**50**

tumour. For instance in W i l l i a m's material this percentage is 23, but among the series published in 1933 or later, in this Finnish material 50, in the others at least 55. The result obtained in Finland, therefore, must be considered as relatively poor.

In the material of mammary gland carcinoma in the male published by W a i n w r i g h t 7 patients had an anamnesis of 20—34 years, while that published by S c h r e i n e r in-

cluded two such patients. It can perhaps be assumed that the enlargement in these cases was originally gynecomastia, and this would tend to confirm the assumption by Gilbert and Geschickter that gynecomastia might be a factor predisposing to mammary gland carcinoma.

The materials of sarcoma in the male breast published in the literature are small. They show that the enlargement has generally been in the breast for a fairly short time only prior to the discovery of the sarcoma, less than 5 years. In one of the two cases of the present material the anamnesis therefore is exceptionally long, over 10 years, in the other it is under 1 year.

The anamneses of benign mammary gland tumours proper in the present Finnish material have varied in duration between 1 month and 50 years, without any characteristic period for the different types of tumours.

TABLE 25. — DURATION OF THE GYNECOMASTIA PRIOR TO OPERATION, ACCORDING TO DIFFERENT INVESTIGATORS

	Total material	Duration of disease < 1 year	
		number	%
Menville	71	51	72
Karsner	236	156	66
Present material	**143**	**92**	**64**

It is seen from Table 25, which apart from the present gynecomastia material includes two series from the literature, that the totals of patients who have consulted a physician within a year of the appearance of the enlargement are slightly higher than the corresponding figures for carcinoma patients quoted in Table 24. However, the difference is apparent only, for, e.g., the difference between the percentages, 64 and 50, of the gynecomastia and carcinoma patients in the present material that have consulted the physician early, applying equations of binomial distribution, is $P_1 - P_2 = 14 \pm 11.9$ %, in other words, the difference between the groups may be coincidental.

III. ANAMNESTIC LOCAL SYMPTOMS AND THOSE FOUND IN THE FIRST EXAMINATION

The enlargement observable in the breast, the main symptom of all the tumours of the male breast, is the same regardless of the type of the tumour. It is of importance, therefore, to try to ascertain whether the patho-anatomical character of the enlargement can be defined from the other local symptoms. — This point has been little discussed in the literature, and no connected investigations could be traced apart from Geschickter's. For this reason all the evidence available on the clinical properties of male mammary enlargements has been collected from the separate publications concerning the different types of male mammary gland tumours. Such investigations have been published e.g. by Schuchardt, Williams, Wainwright, Gilbert, Neal, Sachs and Kappelgaard. It was found that, in almost all these investigations, the most general anamnestic symptom, or that found in the first examination — apart from the enlargement itself — was enlarged lymph nodes in the axilla. Other common symptoms included pain felt in the tumour, adhesion of the tumour to the underlying tissues, intraction of the mamilla, and an ulceration. The last-mentioned symptom obviously was more frequent earlier than it is now, as can be seen from Schuchardt's and William's investigations. This may be due to the fact that patients used to consult a physician at a later stage of the disease than they do now.

The materials of male mammary gland sarcoma found in the literature are small. The clinical picture differs from the carcinoma picture in that, with sarcoma patients no report has been made of a fluid discharge from the papilla, of intracted

mamilla or of any pain felt in the enlargement. The last-mentioned symptom was found in one of the two cases of the present Finnish material, while none of the other symptoms above, nor any ulceration, were found in either of the cases. In one of the cases the enlargement had adhered to the underlying tissues and enlarged lymph nodes were found in the axilla.

Regarding the clinical symptoms of gynecomastia the following observations have been found in the literature: In a certain percentage of cases the gynecomastia has been bilateral, viz. according to Andrews & Kampmeier in 40 %, v. Numers in 7 %, Menville in 13 % and Karsner in 4 %. No sanguineous discharge from the papilla has been found, but sometimes non-sanguineous fluid (Andrews & Kampmeier, Sullivan & Munslow). Nor has any ulceration been reported in gynecomastia. Tenderness was found frequently (Andrews & Kampmeier, Semb, v. Numers, Menville), enlarged lymph nodes in the axilla seldom only (Andrews & Kampmeier, v. Numers).

A review of the clinical local symptoms observed at the discovery of the disease in the different mammary gland tumours of the present material, gave the following finding: — The size of the enlargements, both in the malignant mammary gland tumours and in gynecomastia, has varied within the same limits, from the size of the end of the little finger to that of two fists; however, the benign tumours proper did not include any of the smallest sizes. — Three different types of consistency have been distinguished in the enlargements: hard, firm and soft. The gynecomastia enlargement was hard fairly often (in 29 cases out of 116) and only seldom soft (in 8 cases). The malignant tumours were hard relatively more frequently (in 10 cases out of 22), but in one case even a malignant tumour was soft. Benign tumours, as far as could be ascertained, had not been hard in consistency (3 examined cases). — Both malignant tumours (13 out of 19) and gynecomastia enlargements (35 out of 54) more frequently adhered to the skin than were distinctly detached, and both types were

more frequently detached from the underlying tissue than fixed to it (the malignant tumours in 13 cases out of 19, gynecomastia enlargements in 30 cases out of 32). — The mamilla was intracted in 3 out of 18 cases of malignant tumour, and in 3 out of 155 gynecomastia cases — hence relatively much more often in the previous group. — An ulceration was present in 6 out of 24 malignant tumours, but not in a single one of the 155 gynecomastia cases examined. — Sanguineous discharge from the papilla was observed with one of the 23 carcinoma patients, but never with those suffering from a benign tumour (6 examined cases) or with gynecomastia patients (122 examined cases). However, a non-sanguineous discharge from the papilla had never occured in connection with tumours (26 examined cases) though this had occured in 14 out of the 119 gynecomastia cases. — Tenderness to palpation was a common symptom in the malignant tumours of the male breast (in 11 out of 19 cases) and especially in gynecomastia (in 106 cases out of 130). The enlargement was bilateral in 26 cases and unilateral in 132 cases of gynecomastia. The male mammary gland carcinoma was always unilateral, but in one case it occured in one of the enlarged breasts of a patient with bilateral gynecomastia. Enlarged lymph nodes in the axilla were present in 10 malignant tumours out of a total of 22, and fairly frequently in gynecomastia also, 25 cases out of 110. Enlarged lymph nodes occured in the fossa supraclavicularis with two mammary gland carcinoma cases, but were never mentioned in connection with the benign mammary gland tumours or gynecomastia cases.

In the present investigation *the most common symptom of malignant tumours of the male breast — primarily of carcinoma as the sarcoma cases totalled two only, was found to be tenderness to palpation, and the second commonest enlarged lymph nodes in the axilla; a fairly common symptom, in addition was the adhesion of the enlargement to the underlying tissues.* These findings are in compliance with those reported in the literature. In addition, the other symptoms of the malignant tumours of the male breast found in the present

investigation, as regards type and incidence, are also similar to those mentioned in the literature.

Benign tumours of the male breast are so few, both in the literature and in the present material, that no special conclusions can be drawn as to their clinical picture.

As regards the type and incidence of the clinical properties of gynecomastia, the findings of the present investigation are approximately identical with those discovered in investigations reported in the literature. Furthermore it has been possible to add certain features to the clinical picture of gynecomastia, features to which no considerable attention has generally been paid in the literature. For instance, it was found that the consistency of gynecomastia fairly often, in 25 % of the cases, was hard, and soft only in 7 %; in the remaining cases the consistency was described as firm. In addition, it was found that the gynecomastia enlargement in the majority of cases (65 %) was clearly attached to the skin, in the first place to the mamilla, and that the mamilla in 3 cases was even intracted. It was also found on a couple of occasions that the enlargement was attached to the underlying tissues. — Enlarged lymph nodes in the axilla were found more often in the present material than in the materials reported in the literature, viz. in 23 %.

TABLE 26. — DURATION OF ANAMNESIS IN CASES OF GYNECOMASTIA OF »HARD» CONSISTENCY COMPARED WITH THE TOTAL MATERIAL

Duration of anamnesis	Total material	»Hard» cases
$\leqq$ 3 months	65	13
> 3 months, < 1 year	27	4
$\geqq$ 1 year	51	6

As it was previously (cf. p. 48) found in the present investigation that in gynecomastia the connective tissue becomes denser the older the enlargement, it was considered necessary to check whether the consistency of the gynecomastia enlargement behaves in the same way. For this reason Table 26 specifies the numbers of fresh and old enlargements in the

TABLE 27. — DISTRIBUTION OF GYNECOMASTIA CASES OF »HARD» CONSISTENCY OVER THE DIFFERENT AGE GROUPS COMPARED WITH THE TOTAL MATERIAL

	Age of patients in years at the moment of examination							Total
	10—19	20—29	30—39	40—49	50—59	60—69	70—79	
All cases	21	55	24	13	20	21	13	168
»Hard» cases	2	4	4	3	5	5	4	27

total gynecomastia material on the one hand, and among the enlargements of »hard» consistency on the other. It can be seen from the table that in the latter group most of the cases are fresh, whereas in the total material the fresh enlargements are somewhat less frequent than the others. Hence, *the »hardness» of a gynecomastia enlargement is no indication of the time it has been in the patient's breast.* — A study was made at the same time of whether the enlargements might be of »hard» consistency relatively more often in patients of more advanced age than with younger patients; Table 27 gives parallelly the distribution of the total gynecomastia material and of the »hard» gynecomastia cases by the different age groups. It can be seen from the table that no statistically significant difference obtains between the groups in this respect ($P_1—P_2=19.3\pm10.3$ %), and hence, *the consistency of the gynecomastia enlargement is »hard» no more frequently with patients of advanced age than with younger patients.*

Differential diagnosis of the tumours of the male breast

The differential diagnosis of the tumours of the male breast according to S e m b, should encounter no difficulties. On the other hand, M e n v i l l e and G e s c h i c k t e r are of the opinion that the differential diagnosis is not easy if the enlargement is distinctly defined and the patient middle-aged. According to the latter investigators, the enlargement is likely to be benign if bilateral, also — according to M e n v i l l e — if its size has varied and, according to G e s c h i c k t e r, if the patient is under 21 years.

The preceding chapter, on the clinical local symptoms of enlargements of the male breast, showed that *the symptoms of the initial stages of malignant mammary gland tumours of the male and of gynecomastia are quite similar:* Gynecomastia patients may be of advanced age. The gynecomastia breast is often hard in consistency, in most cases attached to the skin, sometimes even to the underlying tissues. In some cases of gynecomastia the mamilla is intracted. In gynecomastia there are fairly often enlarged lymph nodes in the axilla. A malignant tumour of the breast has often been tender to palpation. — Hence, the differential diagnosis of these mammary gland tumours may often be impossible on the basis of clinical symptoms alone, and in that respect the present author agrees fully with M e n v i l l e and G e s c h i c k t e r. But estimation of the demarcation of the enlargement, which M e n v i l l e and G e s c h i c k t e r considered possible, cannot be achieved with the present material. Firstly, it was established previously (p. 33) that a capsule is practically never found in gyneco-

mastia, and secondly, observations on the consistency of male mammary gland tumours show (p. 79) how difficult it is to distinguish by this means between malignant tumours of the male breast and gynecomastia. — How difficult a differential diagnosis of tumours of the male breast may be was also seen when the patho-anatomical diagnoses of the present Finnish material were compared with the diagnoses made by the physicians submitting the biopsy specimens. It was found that a malignant tumour was considered benign, admittedly once only, and a benign growth proper as malignant once only, whereas gynecomastia, on several occasions, viz. in 39 out of 185 cases, was diagnosed as a malignant tumour.

However, in the present material, *even clinical differences have been found between malignant tumours of the male breast and gynecomastia.* For instance, the tumour patients are generally of advanced age — the youngest in the present material being 39 — while the majority of gynecomastia patients are under 39. The consistency of the tumours is hard more often than in gynecomastia, and the tumour is also more often attached to the underlying tissue. Enlarged lymph nodes in the axilla are relatively more frequent with malignant tumours of the male breast than in gynecomastia, but in the present material at least the difference is not statistically significant; the difference between the incidence probabialities of enlarged lymph nodes in the axilla, $P_1 - P_2 = 22 \pm 11.3$ %, and as this difference is smaller than twice its mean error, the difference between the groups may be coincidental. — In gynecomastia an ulceration or sanguineous discharge from the papilla, such as takes place in the male mammary gland carcinoma, was not found a single time; nor was a non-sanguineous discharge from the papilla ever found in the malignant mammary tumours in the present material, as it was sometimes in gynecomastia; according to the literature this rare phenomenon has sometimes been seen even in connection with mammary gland carcinoma of the male. As far as is known, male mammary gland carcinoma is never bilateral, as gynecomastia quite often is — in 16 % of the present material. On the other hand, in one of the carcinoma cases

in the material carcinoma developed in one of the enlarged breasts of a man suffering from bilateral gynecomastia.

Hence, the conclusion arrived at in the present investigation is that *if a man with a unilateral or bilateral mammary gland enlargement is under 30, and the enlargement displays no ulceration and no sanguineous discharge from the papilla, it is practically certain that no malignant tumour is in question. If, again, ulceration is present in the male mammary gland enlargement, or if the papilla has bled, a carcinoma is definitely in question. In all the other cases the differential diagnosis on the basis of clinical findings is more or less uncertain, and a patho-anatomical examination must be considered indispensable to confirm the diagnosis.*

Treatment of the tumours of the male breast, and the therapeutic results

As the importance of treatment in malignant tumours of the male breast is quite different from that in benign tumours and as, on the other hand, the most important thing in planning the treatment for the latter is the extent to which they tend to become malignant, it has been considered necessary to review the treatment of the tumours of the male breast and the therapeutical results separately for each group.

I. TREATMENT OF THE MALIGNANT TUMOURS OF THE MALE BREAST, AND THE THERAPEUTICAL RESULTS

Earlier investigators, such as Williams, Finsterer and Judd & Morse had no roentgen at their disposal, and in their cases the therapeutic measures were solely operative. Judd & Morse's patients were all treated with a radical operation, while a number of Williams's and Finsterer's patients were treated with extirpation or ablation, others, including one of these, by evacuating the axilla.

A considerable part of the patients of the later investigators were treated with roentgen rays only; these cases, apart from two of Gilbert's patients, were all in an advanced stage of the disease. One of these patients of Gilbert died the same year, another was still alive a year after discovery of the disease. The other patients in Gilbert's series and all those in Schreiner's and Kappelgaard's materials that had been treated with roentgen rays only, had a relapse or metastasis within three years of the discovery of the disease; no information in this respect is available on Sach's material. — A minor part of Gilbert's, Sach's and Kappelgaard's cases were treated operatively only, but the majority had received roentgen treatment in addition; of Schreiner's cases not a single one was treated operatively only. — In Schreiner's material the operative measure has always been local only, and even in Williams's material this is true of nearly two-thirds of the cases. In the other materials, again, at least half the operatively treated patients had been subjected to a fairly radical operation, i.e. in addition to the removal of the tumour at least the axilla was evacuated.

In the present Finnish material a fairly radical operation has been employed in the operative treatment of a minor part of the carcinomas only (9 out of 22 cases), in the majority of the cases (12) only local measures, either alone (3 cases) or together with roentgen treatment. One patient only was treated with roentgen rays alone, although it must be taken into consideration that in four cases the operative measure was, in the first place, diagnostic only.

None of the patients in the above-mentioned materials of male mammary gland carcinoma was treated with orchidectomy, employed by Farrow & Adair in such a case. These investigators reported that the tumour, ulceration and bone metastases decreased after orchidectomy.

TABLE 28. — RESULTS OF TREATMENT OF CARCINOMA OF THE MALE BREAST IN THE DIFFERENT MATERIALS

	Number of cases in wich a follow-up examination was effected	Number of cases inoperable at the outset	Free from relapse or metastasis after		
			3—5 years number	5 years	
				number	%
Williams 1889	17			2	12
Finsterer 1906	9	2	0	1	11
Gilbert 1933	46	28	2	5	11
Sachs 1941	155			15	8
Kappelgaard 1944	48	19	4	10	21
Present material	**22**	**5**	**2**	**3**	**14**

Table 28 gives the therapeutic results by the different investigators and also the number of cases that were originally found inoperable in each material, where recorded. The table shows that the best therapeutical result was obtained in Kappelgaard's Danish material: 21 % of the patients remained healthy 5 years after the treatment, in spite of a consider-

able number of the cases being originally inoperable. On the other hand, it is found that the results in the newer materials, apart from Kappelgaard's material, have been no better than in the older ones, in spite of roentgen treatment facilities. It is true that in the older materials follow-up examinations were fairly rare. — *Treatment results with the present Finnish material are similar to those observed in any other material in the table: 14 % of the patients were living 5 years after treatment.* Compared e.g. with Kappelgaard's material the difference is statistically insignificant, as the difference between the probabilities of 5-year recovery, $P_1 - P_2 = 7 \pm 9.4$ %.

To judge the effect of therapeutic measures on the results a study was also made of how the patients who remained healthy for 5 years were treated in the materials published in the literature. Unfortunately the investigations where this is recorded are very few and very limited: Williams (2 cases), Poulsen (1 case), Finsterer (1 case), Judd & Morse (1 case) and Gilbert (5 cases). — 6 patients out of 10 were treated with a fairly radical operation and 5 of them, in addition, received roentgen treatment. Three patients were treated with a local operation and roentgen rays and one with a local operation only. — Patients with 5-year recovery in this material were treated as follows: One (healthy 10½ years) with radical operation and both pre- and post-operative roentgen therapy, one (healthy 6 years) with Exstirp.tumoris et evac.axillae and post-operative roentgen therapy and one (healthy 5 years 10 months) with Ablatio mammae and post-operative roentgen therapy.

Investigations reporting on the methods and results of treatment of male mammary gland sarcoma are very few, and their materials are small: Finsterer (11 cases), Schreiner (1 case), Fox (2 cases) and Rose (2 cases). Of these, no follow-up examinations were made in Finsterer's material. In most cases the patients underwent a local ectomy only, and in a single case the patient was treated with roentgen rays; none were treated with roentgen rays alone. Of the 5 cases in which a follow-up examination was made, 4 remained

healthy 5 years after the operation. — Of the sarcoma patients in the present Finnish material, one was treated with a radical operation and no roentgen; he had a relapse after 4 months and died 14 months after the discovery of the disease. The other was treated with Ablatio mammae and received post-operative roentgen therapy; he died 7 years after the discovery of the disease, of metastasis.

Among the patients of the present material suffering from mammary gland carcinoma, 7 were treated operatively only, and a single case (originally inoperable) with roentgen rays only. 14 of the operated patients received post-operative and 2 both pre- and post-operative roentgen therapy. The operative measure was in 4 cases Excisio explorativa, in 5 Exstirpatio tumoris, in 3 Ablatio mammae, in 2 Exstirp. tumor. et evacuatio axillae, and in 7 cases Operatio radicalis. — 7 patients remained healthy for 2 years — 10½ years after the operation; of them, a total of 5 patients lived at least 3 years after the operation and 3 of them over 5 years (10½ and 6 years and 5 years 10 months). — Of the 5 patients that remained healthy for 3 years or more after treatment, 4 were treated with a fairly radical operation and 3 of them with roentgen rays in addition; the fifth patient underwent a local operation only (Ablatio mammae) and subsequent roentgen therapy. — The relapses occurred 3 months — 5 years after the discovery of the disease in the 9 patients on which this information was available. Of the total of 12 patients who had a relapse after treatment, 5 were originally treated with a fairly radical operation, and 2 of them with roentgen rays as well. In the remaining 7 cases the operative measure was local only, and 5 of them received roentgen therapy in addition. — The cases inoperable at the discovery of the disease were treated as follows: one received roentgen therapy only, and on one an Excisio explorativa only was performed; 2 were treated with Excisio explorativa and roentgen rays, and in one case the tumour was removed and roentgen therapy given in addition. All the 5 died within 4—18 months of the discovery of the disease. — The 14 patients who died of malignant tumour (this was the cause of death in all the fatal

cases of the present material) lived for 4 months — 6 years 5 months, or an average of 2 years 2 months, after the discovery of the disease.

Of the 7 relapses of mammary gland carcinoma in the present material. of which the method of treatment is known, 6 could be treated, and of these 5 only could be operated on. 2 patients only recovered from their relapse, the others died 9 months to 6 years 5 months after the discovery of the disease. One of the patients who recovered was treated with Exstirpatio tumoris recidivantis et evacuatio axillae and with roentgen rays, and the patient has continued healthy since for 5 years 2 months. The other was treated with radical operation and roentgen rays, and has continued healthy for 2 years 1 month.

It can be established, therefore, that *the prognosis of male mammary gland carcinoma is generally poor, and seems to have been affected but little by the introduction of roentgen therapy*. For instance, of Mustakallio's Finnish material of female mammary gland cancer treated with radical operation, the 5-year survivals constituted 38 %, and of those treated with extirpation of tumour plus roentgen the result was percentually better still (7 cases out of 8). In Pylkkänen's material of female mammary gland cancer, 25 % treated with radical operation come in the 5-year survival group and 37 % of those treated with radical operation plus roentgen. — It is also found that in the newer materials of male mammary carcinoma in the literature, firstly, the patients consulted the physician at a sligthly earlier stage of the disease, and secondly, the tendency has been to treat the patients with a fairly radical operation, i.e. in addition to the removal of the tumour at least the axilla has been evacuated, and by combining roentgen treatment with the operation. In contrast to this, in over half the operatively treated cases of the present Finnish material the operation has been local only, though most of the operated patients received roentgen treatment in addition to operation. — Of the patients with a 5-year survival rate reported in the literature, the majority recovered after a fairly radical operation, on the one hand, and after roentgen treatment combined with the

operation. on the other, but never after roentgen treatment alone. The same applies to the 3-year and 5-year survival groups in the present Finnish material. — In addition it seems that, considering the location of the relapses and metastases, the two relapse cases of the present material that could be restored to health would perhaps not have suffered a relapse — at least not as soon as they did — if the surgical treatment had been radical at the outset and not merely local.

It therefore seems that, *in treatment of carcinoma of the male breast, roentgen treatment has been unable to replace radical operative treatment, and that radical operative treatment must still be considered as the most important therapeutic measure with which roentgen therapy must be combined.* — Judged by the present Finnish material, *the prospects of treating a relapse and metastasis of male mammary gland carcinoma seem fairly small.*

There are very few reports in the literature on cases of sarcoma of the male breast where follow-up examinations have been effected. Judged by these few, however, it seems possible that the prognosis for male mammary gland sarcoma might be slightly better than for carcinoma. The present material does not support this opinion but it contains only two cases. According to the literature, the radicalness of the operative treatment in male mammary gland sarcoma is not as important as in carcinoma; no conclusions can be drawn in this respect on the basis of the present Finnish material.

II. TREATMENT OF BENIGN TUMOURS OF THE MALE BREAST, AND THE THERAPEUTIC RESULTS

According to the literature the only benign tumour of the male breast found to have degenerated malignantly is duct papilloma (Erdheim, Martin); it has also been found to recur (David). For these reasons papilloma of the male breast has been treated with major operations, such as Ablatio mammae et evacuatio axillae (Greenough & Simmons).

As regards the treatment of other benign tumours of the male breast, a simple removal of the tumour has generally been considered adequate in the literature (Neal & Simpson, Johnston, Geschickter).

The benign tumours in the present material, which did not include a single papilloma, were treated operatively only, with a simple removal of the tumour. A follow-up examination was made with two patients, both of whom were found healthy; — one, who had had haemangioma, 3 years, and the other, who had had lipoma, 5 years after the operation.

Bearing in mind the generally known tendency of papillomas to malignant degeneration and relapse, it seems that it might be appropriate to treat them more radically than by mere extirpation; a resonable measure would be to effect at least Ablatio mammae, and, besides, observe the patient afterwards. If, again, malignancy is found in the papilloma, it would be logical to treat it like the carcinoma it is. — As regards the treatment of other benign tumours of the male breast, simple removal of the tumour is obviously adequate.

III. TREATMENT OF GYNECOMASTIA, AND THE THERAPEUTIC RESULTS

The treatment of gynecomastia, and expressly the therapeutic results, have generally been fairly concisely dealt with in the literature.

Some investigators, such as Andrews & Kampmeier, Erdheim, Hoffman and Geschickter, pointed out in their survey of the treatment of gynecomastia that the disease might have a considerable tendency to spontaneous regression, particularly when the patients are young. Karsner doubted this. — Andrews & Kampmeier and Karsner did not consider the treatment of gynecomastia at all important. The majority of the investigators, however, have been of the opinion that treatment of gynecomastia is to be recommended; most of them, viz. Erdheim, Semb, Sullivan & Munslow and Geschickter for the reason that gynecomastia may cause psychic or physical suffering for the patient, Menville because he found it to some extent advisable to consider the possibility that gynecomastia may sometimes degenerate malignantly. — In addition, Menville and Geschickter pointed out that a differential diagnosis between gynecomastia and a malignant tumour may not be possible purely clinically when the enlargement is firm and distinctly defined, but that patho-anatomical examination, i.e. surgical treatment, is then necessary. — Geschickter emphasised that if gynecomastia is caused by some distinctly discernible factor, i.e. by a testicular or adrenal tumour, its removal is essential

and at the same time constitutes effective treatment of the gynecomastia also. — Hoffman has treated 28 gynecomastia patients with testosterone — the majority of his cases, 19, were under 20 years of age — and reported having been able to cure the disease in all but two of the cases; at least two of the patients, it is true, had a relapse. On the other hand, Geschickter and Sullivan & Munslow had no positive results from treating gynecomastia with testosterone. — Menville treated some gynecomastia patients with roentgen rays and concluded that this procedure may be helpful in fresh cases. — However, when gynecomastia has been treated, the treatment has usually been surgical, and the majority of the investigators have not considered it an important point whether the mamilla has been removed at the same time or left (Erdheim, Semb, Menville, Geschickter, Karsner), and e.g. Sullivan & Munslow effected the ectomy leaving the mamilla intact.

With the exception of a few individual cases, no follow-up examinations regarding the results of treatment in gynecomastia have been found in the literature, apart from the remark by Menville and Geschickter that no malignant degeneration had been apparent in their cases of gynecomastia; however, they did not state the number of cases in which a follow-up examination had been made, nor the length of observation period.

In the present Finnish gynecomastia material of 185 patients, the enlargement only had been removed in 146 cases, preserving the mamilla, while in 28 cases the mamilla had been removed together with the enlargement. — 3 patients, on whom an Exstirpatio tumoris was performed, also received roentgen treatment. One of them, with bilateral gynecomastia, was first given roentgen treatment, but as that did not help an extirpation was performed; this patient had had gynecomastia for 10 years in one breast, 2 years in the other. In 2 cases roentgen was given post-operatively for tenderness, as glandular tissue was assumed to have remained after the operation. The fact that the above case, the only one in the present material that was originally treated with roentgen, did

not respond to this treatment, complies with Menville's observations that roentgen therapy has no effect on old gynecomastia enlargements. — No single case in the present Finnish material was treated with roentgen only, nor was any case treated with testosterone. — No treatment was begun in the case of a 68-year old gynecomastia patient, and after a year the enlargement had disappeared by itself.

Of the gynecomastia patients of the present Finnish material, 97 were observed for a minimum of 6 months after treatment; the observation period was $\geq$ 10 years in 6 cases, $\geq$ 5 years in a total of 23 cases, $\geq$ 2 years in a total of 57 cases, and $\geq$ 1 year in a total of 86 cases. There was a recurrence in 9 cases. All the relapses appeared within 2 years of the operation, 6 of them appeared within 1 year and 4 within 6 months. All the relapses occurred after minor operations only, viz. Excisio explorativa and Exstirpatio, and probably for the reason that some mammary gland tissue remained after the operation. — Treatment of relapses was effected in 7 cases only: Extirpation was performed on 4 patients; one of them is healthy 5 and one 3 years after the operation, while nothing is known of 2. Ablatio mammae was performed on one, and he was healthy 4 years later. In one case Ablatio mammae et evacuatio axillae was performed, and one received only roentgen treatment for his relapse; these two patients have not been traced. Two recurring enlargements were not treated at all, and they have remained unchanged, one for 6 years, the other for 4.

Spontaneous regression of gynecomastia, which some investigators (p. 94) regarded as fairly common, at least does not seem to be regular and rapid, for although this was found to have taken place in one of the cases of the present Finnish material, the anamnesis, in the 143 operated cases of the present material in which the duration of the disease is known, has been $\geq$ 1 year in a total of 51 cases, $\geq$ 3 years in a total of 20 cases and $\geq$ 5 years in a total of 12 cases. Furthermore, it is to be noted that the two recurrences of gynecomastia that had not been treated remained unchanged for 6 years and 4 years, respectively.

As regards the indications for operation in the gynecomastia cases of the present Finnish material, in 39 out of the 184 operated cases, as mentioned on p. 84, the enlargement was originally, to some extent at least, suspected to be malignant. However, it is apparent that more often still, viz. generally *when the gynecomastia patient has been old or middle-aged, the uncertainty of the clinical diagnosis has been the main indication for operation. — With younger patients in the material, the gynecomastia enlargement has probably been removed primarily due to its having caused psychic or physical suffering to the patient.* Indicative of this is that in these cases the operation has not been performed immediately, for the pre-operative duration of the disease with the 61 patients under 30 in the present material, where the length of gynecomastia anamnesis is known, has been $\geq$ 1 year in 36 cases and $\geq$ 3 months in only 17 cases.

The fact that all the recurrences of gynecomastia occurring after operation applied to operation where the mamilla was retained seems to indicate that the *extirpation of mammary gland tissue without removing the mamilla is not quite simple technically, and that Ablatio mammae would be a more suitable procedure for this purpose.* — However, as the result of the operative treatment of gynecomastia generally has been good even when the mamilla has been left, and as operation is a fairly minor procedure for the treatment of gynecomastia and, furthermore, leads quickly to the desired result, it is understandable that the lengthier and more expensive testosterone treatment has not been tried with any of the patients in the present material.

The previously mentioned case of V.V.P. in the present material, in whom a testicular tumour was found a year after the discovery of bilateral gynecomastia, and which tumour on operation was found to be malignant, seems to indicate that *it would be advisable generally to palpate the testes of each gynecomastia patient* for such a possibility.

Survey of the theoretical and practical significance of tumours of the male breast

As reported previously in the present investigation, the male mammary gland, normally a rudiment, may become enlarged due to a tumour proper developing in it; both benign and malignant tumours, with a majority of the latter, have been found in the male breast.

In the majority of the cases, however, the »normal» rudimentary male mammary gland becomes enlarged through hypertrophy; in such a case the growth of both connective tissue and epithelium, i.e. fibro-epithelial hyperplasia, is always in question, and the mammary gland enlargement of this origin is termed gynecomastia.

When transformed into gynecomastia, the »normal» mammary gland of the male obtains additional features reminiscent of the female breast, mainly of two different types: an exterior appearance somewhat reminiscent of it, and a somewhat more developed lobular and acinar structure than that present in the »normal» male mammary gland.

Patho-anatomically gynecomastia is somewhat reminiscent of female Mastopathia cystica. However, there is an essential difference: The main element in the former, as in the »normal» male mammary gland, is still connective tissue, whereas the essential element in female Mastopathia cystica consists of a developed system of lobuli and acini. — Obviously it is this difference that accounts for fibroadenoma apparently never having been found in the male mammary gland, although it is fairly common in the normal female breast, and not in-

frequently seen in connection with female Mastopathia cystica, as has been established e.g. by S e m b.

The character of the »normal» mammary gland of the male does not, therefore, even when it is enlarged into gynecomastia, assume such a resemblance to the female mammary gland that fibroadenoma might develop in it. As carcinoma, in contrast to fibroadenoma, has been found in the male mammary gland, and although in the majority of cases it has developed in the »normal» mammary gland of the male, several investigators have been interested in the question of whether carcinoma can develop more easily in an enlarged male breast, gynecomastia, than in a »normal» one. — Carcinoma has in fact been found to develop now and again in a gynecomastia breast, e.g. in one of the cases in the present material. — In addition, epithelial proliferation is often, in some 50 % of the cases in this material, found in gynecomastia, and microscopic and even macroscopic papillomas sometimes. — In other words phenomena which are generally considered to indicate a slightly greater succeptibility to malignant degeneration than is possessed by the regular epithelium. — On the one hand, however, the main part of male mammary gland carcinomas has developed in a mammary gland of normal size, and on the other, no malignant degeneration has been found in the follow-up examinations of some gynecomastia materials. — *Hence, there is so far no direct evidence that a gynecomastia breast is more susceptible to carcinoma than the »normal» male mammary gland, but neither is there any evidence to the contrary. It must be concluded, therefore, that this question still awaits a final answer, either affirmative or negative.*

However, as it has not been possible definitely to exclude the possibility that a gynecomastia breast might be somewhat more susceptible to malignant degeneration than the »normal» male mammary gland, the practical conclusion to be drawn is probably that it is preferable to be too active than too conservative in the treatment of gynecomastia. — Operation as a therapeutic measure for gynecomastia is fairly simple, safe and leads to quick results, relieves the patient in his psychic

and physical suffering and, in addition, provides the possibility of patho-anatomical diagnosis. Hence it seems to be an advantageous therapeutic method for gynecomastia, and, at least when the patient is over 30, the best one. — Insofar as there is no special reason to save the mamilla, it may be best to remove it at the same time as the glandular tissue, for it is technically easier to remove the glandular tissue in its entirety by this procedure than if the male mamilla is retained, and thus recurrences are avoided. — Another factor in favour of ablation as the treatment for gynecomastia is, further, that the skin covering the gynecomastia breast probably constitutes an essential part of such an enlarged male mammary gland, for the gynecomastia enlargement, in the present material too, was often found attached to the skin (in 35 out of 54 examined cases). It may also be mentioned in this connection that Perä s a l o has recently shown that no distinct demarcation exists in the female breast between the glandular tissue and the skin, and that the glandular tissue may sometimes extend right to the skin.

The conclusion reached in the present investigation is that a radical operation combined with roentgen treatment is the most advantageous therapeutical measure for male mammary gland carcinoma. The above observations on the close connection between the mammary gland tissue and the skin covering it, and the observation, made in the present investigation too, that some male mammary gland carcinomas in their cell type are reminiscent of cutaneous cells (Carcinoma basocellulare, Carcinoma spinocellulare), tend to emphasise the importance of the removal of an adequate amount of skin when operating on a carcinoma in the male, as well as in the female, breast.

The practical result from the above is that a *reasonably radical attitude towards gynecomastia and a severely radical approach to male mammary gland carcinoma are the best lines to adopt as regards treatment.*

Summary and Conclusions

The investigation is based on a patho-anatomically examined material of 221 different tumours of the male breast. — Clinical data are based on the sources specified in Table 1.

The following replies can be given to the questions posed in the introduction defining the object of the investigation.

1. The material includes 185 cases of gynecomastia = 84 %, 22 cases of carcinoma = 10 %, 2 cases of sarcoma = 1 %, 9 cases of benign tumours proper = 4 % and 3 cases of inflammatory formations = 1 %. It has been found that of the mammary gland carcinoma cases in Finland 1.1 % are males. Of the malignant mammary gland tumours found in Finland sarcoma is probably relatively more frequent in men than in women.

2. Malignant tumours: — The commonest type of carcinoma in the material was found to be Carcinoma solidum, followed by Adenocarcinoma and, in the third place, by covering epithelium carcinoma. The material contains one case of Carcinoma Paget. — Estimating the content of ribose polynucleotides in the cytoplasm of the carcinoma cells by the basophilia of the cytoplasm, its quantity seems to be greater the more active the cells. — No free metachromatic substance and mast cells generally were found in carcinoma tissue. — The two cases of sarcoma in the material were fibrosarcomas. No free metachromatic substance and no mast cells were found in them.

Benign tumours proper: — These are rare in the material. The types are: Lipoma (commonest), fibrolipoma, haemangioma, angiofibroma and dermoid cyst. Not a single benign

fibro-epithelial tumour of the male breast was found, but it was established that in the original patho-anatomical investigation gynecomastia had often been diagnosed as fibroadenoma. It was concluded that a duct papilloma may sometimes be found in the male mammary gland, but no fibroadenoma, or at least very seldom only.

Inflammatory formations: — These were found to be the least common of male mammary gland enlargements, with a total of three cases in the present material: Tub. mammae, simple abscess, and actinomycosis.

Gynecomastia: — On the basis of the facts reported the conclusion arrived at is that benign chronic fibro-epithelial enlargements of the male breast, apart from some rare benign tumours, apparently are, all of them, similar diffuse formations. They are not tumours proper, show no variation according to the patient's age, nor does there seem to be any difference according to etiology. It has been possible to confirm the general conception that gynecomastia consists in the main of connective tissue, and there are two different types: fibrous stroma connective tissue present in all cases and usually constituting the main part of the connective tissue, and loose periductal »mantle connective tissue» not present in all cases. — It has been found that hyaline degeneration of the connective tissue is a phenomenon common in gynecomastia, and that its presence is not dependent on the age of the patient or of the enlargement. — It has been shown that »mantle connective tissue» is young, newly-formed connective tissue; it contains plenty of free metachromatic substance and mast cells, both of which are found practically nowhere else. The connective tissue as a whole in gynecomastia becomes more fibrous the older the enlargement. — Cysts have been found in 86 % of the gynecomastia preparations, in the majority of cases as dilatations of ducts, less frequently of the acini. In gynecomastia the fibro-epithelial growth process and the formation of secretion apparently constitute factors accounting for the origination of the cysts. — In a good 10 % of the gynecomastia cases in the material lobular structure has been found, while acini were observed a little more frequently. — The

epithelium in gynecomastia is usually 2-layered, sometimes 1-layered, and seldom only 3-layered. Proliferation in the epithelium was found in nearly 50 % of the cases, while 5 preparations revealed a microscopic papilloma. The basal membrane is distinct in all the gynecomastia cases of the present material. — The epithelial cells, in some 70 % of the gynecomastia preparations, are mostly cuboidal, in about a quarter mostly cylindrical, and seldom only mostly flat. In the nuclei of the epithelial cells the Feulgen reaction is distinct; the cytoplasm of the cells generally stained with methylene blue to display intense basophilia. »Pale epithelium» was found in 19 out of 183 gynecomastia cases of the material. Its cytoplasm does not stain with methylene blue to reveal basophilia, and judged by this, it does not contain any considerable amount of ribose polynucleotides; the Feulgen reaction is distinct in the nuclei. — In 11 cases of gynecomastia so-called »intermediate epithelium» is found, which morphologically and in the ribose polynucleotides content of its cytoplasm is an intermediate form between the »pale» and the ordinary mammary gland epithelium. The »pale» and »intermediate» epithelium are more closely related mutually than to the ordinary mammary gland epithelium, and very probably more closely related to the cylindrical mammary gland epithelium than to the cuboidal. It seems as if the »pale», »intermediate» and cylindrical epithelium were an involution phenomenon in gynecomastia, and as if the involution of the glandular cell in gynecomastia begins with a morphological change of the cell, with which is connected disappearance of ribose polynucleotides from the cellular cytoplasm. — Cell-free secretion was found in the lumen of the glandular ducts in some 70 % of the cases; the secretion was mostly acidophilic, sometimes basophilic. In nearly half the cases desquamated epithelial cells were also present in the ducts; in some preparations desquamated epithelial cells but no cell-free secretion was seen in the ducts. — In gynecomastia the epithelial cells both of the ducts and of the acini possess a secretory ability. — Apocrine sweat glands were found in 21 out of 183 cases of the material, and in all age

groups; they were more frequent in fresh gynecomastia enlargements than in old ones, in contrast to the »pale» epithelium, which they resemble morphologically. — Eccrine sweat glands were found only in five of the gynecomastia cases of the material. — In all the gynecomastia cases of the present material »inflammation cells» were found, mainly in the periductal connective tissue; in some 85 % they were scant, and fairly abundant in about 1 % only. They were generally mononuclear, the main part consisting of lymphocytes, a part of mast cells, and a small amount of plasma cells; even polymorphonuclear cells were seen sometimes. The inflammation cells observed probably generally do not indicate an inflammation in gynecomastia but are apparently an expression of intensified blood circulation connected with the growth of tissue and resorption of secretion and of degenerating cells. — As the investigation revealed that the glandular ducts grow at the same time as the connective tissue, and as epithelial proliferation was often discovered in the ducts, gynecomastia is in its nature fibroepithelial hyperplasia of the male mammary gland. In this respect it is a process patho-anatomically similar to female Mastopathia cystica. But essential differences exist: A gynecomastia breast seldom bears any close resemblance to a female breast in its outward appearance. The microscopic basic element in gynecomastia is connective tissue, and in it lobular structure and acini are fairly rare, whereas in female Mastopathia cystica the conditions are practically reversed. This is also indicated by the fact that in gynecomastia the cysts develop mostly from the glandular ducts, in female Mastopathia cystica generally from the acini. Gynecomastia develops from the enlarging of a rudimentary organ, female Mastopathia cystica from the degeneration of normal female breast capable of functioning. It seems desirable, therefore, to use a special term for the diffuse chronic fibroepithelial enlargements of the male breast, and the most appropriate term seems to be »gynecomastia».

3. It has not been possible in the present investigation to suggest factors that could throw light on the etiology of the malignant or benign tumours proper of the male breast.

According to the present material gynecomastia appears to have no tendency to malignant degeneration. However, the reservation must be made on this point that in some materials in the literature both numerically and relatively more gynecomastia cases leading to carcinoma have been found than in the present material, which includes one case only. — Regarding the etiology of gynecomastia the following conclusions have been arrived at: Gynecomastia probably is generally not due to hereditary factors, trauma, genital disorder discernible at physical examination, inflammation or any ordinary disease. Its origination seems to depend on some hormonal factors, primarily sexual hormones, for it has been found that the incidence of gynecomastia has been closely connected with the period, on the one hand, of the most intense development and activity, on the other, of the decline of the sexual life of the male; the hair growth of gynecomastia patients was remarkably often, in 39 % of the examined cases, of a feminine type; two of the patients in the material had contracted gynecomastia immediately after stilbestrol medication; in one of the patients a malignant testicular tumour was stated a year after the appearance of bilateral gynecomastia.

4. The material contains so few benign tumours proper of the male breast and the patients concerned have been so defectively examined clinically that no attempt has been made to define the clinical picture of this group. A comparison of the clinical symptoms of the malignant tumours of the male breast and of gynecomastia showed that these symptoms have very often been similar: the size of the enlargement in both groups has varied within the same limits; the tenderness to palpation of the enlargement has been the commonest symptom in both groups; both the malignant tumour and gynecomastia has often been of hard consistency, and the enlargements of both types have infrequently been soft; both malignant tumours and gynecomastia enlargements were often attached to the skin, and the mamilla was sometimes intracted in connection both with a malignant tumour and gynecomastia; in the groups of both malignant tumours and gynecomastia the axillary lymph nodes were often enlarged; the patients with malignant

tumours were generally of advanced age, although the youngest was but 39, but a considerable part of the gynecomastia patients too were over 39, even though the majority were younger. — However, distinct differences have also been discovered between the said groups: in gynecomastia, not a single instance of ulceration or sanguineous discharge from the papilla was found, in contrast to male mammary gland carcinoma, and the secretion of non-sanguineous fluid from the papilla was never found in connection with malignant tumours, but sometimes in gynecomastia; gynecomastia has fairly often been bilateral, which never applied to the mammary gland carcinoma; in one of the cases of the present material carcinoma, however, developed in one of the enlarged mammary glands of a man with bilateral gynecomastia; in two of the carcinoma cases of the present material enlarged lymph nodes were found in the fossa supraclavicularis but in no single case of gynecomastia. — Differential diagnosis between a malignant tumour of the male breast and gynecomastia is often impossible in the initial stage of the disease on the basis of clinical symptoms. However, if a man with a unilateral or bilateral mammary gland enlargement is under 30 years of age, and no ulceration is present in the enlargement or sanguineous discharge from the papilla, it is practically certain that no malignant tumour is in question. If again an ulceration is present in the male mammary gland enlargement or the papilla has bled, the carcinoma diagnosis is certain. In all other cases a patho-anatomic examination is to be considered indispensable to corroborate the diagnosis.

5. *Treatment of malignant tumours:* — 50 % only of the carcinoma patients of the present material consulted a physician within a year of the beginning of the disease. This result is poorer than the corresponding figures in the recent foreign materials. — Out of the 22 carcinoma patients of the material, 5 were inoperable when first examined, which proportion is no worse than in the materials in the literature in general. — In the present material the 5-year survival percentage is 14, or similar to the materials in the literature. — Male mammary gland carcinoma is to be treated primarily with a

radical operation and roentgen, and in the operation plenty of skin is also to be removed. — One of the sarcoma patients in the material was treated with Ablatio mammae plus roentgen, the other with a radical operation without roentgen; the former started a metastasis after 5 years with exitus 2 years later, the latter after 4 months, with exitus 14 months after the operation.

Treatment of benign tumours proper: — Apart from papilloma, extirpation is a suitable measure of treatment for benign tumours proper of the male breast. The papillomas should be treated by Ablatio mammae, and if malignant degeneration is noticed, they should be treated like carcinoma.

Treatment of gynecomastia: — Out of the 185 gynecomastia cases in the material, the enlargement was removed in 149 saving the mamilla, and both were removed in 28 cases, and in 3 cases included in the latter figure even the axillary lymph nodes were removed; on 7 patients an Excisio explorativa only was performed. Roentgen treatment prior to extirpation was given without result to a patient who had had the enlargement in the breast for several years, and to two patients after extirpation for tenderness. A patient of 68 was not treated at all, and after a year the enlargement had disappeared. — Relapse occured in 9 cases, always within 2 years of the operation and only after minor operative measures, never after an Ablatio mammae. — It seems as if the tendency of gynecomastia to spontaneous regression is not very great, or at least not rapid. — When examining a gynecomastia patient it is advisable to palpate his testes for a possible testicular tumour, although this possibility is slight. — The conclusion reached is that an operation as the treatment for gynecomastia is necessary for men over 30 years to corroborate the diagnosis; Ablatio mammae is perhaps to be recommended in preference to an operation saving the mamilla. For younger gynecomastia patients also an operation is the most rapid and cheapest therapeutic measure, and an effective help in their psychic and physical suffering due to mammary gland enlargement, enabling in addition a patho-anatomic examination.

Questionnaire

Please supply the answers to the following questions unless you can see me for a follow-up examination:

Have you had goitre (when?)?

Have you had diabetes (when?)?

Have you had any other severe diseases (if so, what and at what age?)?

Are you married (if so, since when?)?

Have you any children (how many?)?

Are your genitals normally developed (both testes in the scrotum and of normal size, and the penis normal)? If not, how do they differ from the normal?

Have you suffered from any diseases in your genitals (if so, what and at what age?)?

Have you, as an adult, suffered from sexual impotence? If so, at what age?

How often do you usually enjoy sexual intercourse (provided you are married)?

Have you had an enlargement of the prostate or its symptoms (weakened urinary jet, retention of urine)? If so, at what age, and how has it been treated?

Have your parents, their parents, brothers or sisters, or your own brothers and sisters had tumours of any kind (if so, what kind?)?

Have you yourself previously had other tumours (if so, what kind and when?)?

How long did you have the breast tumour in question before it was operated on? Did you, prior to the appearance of the

tumour, hurt yourself once, or several times, in the breast where the tumour then appeared (if so, when and how?)?
In which breast was the tumour? Was the other breast healthy (if not, what was wrong with it?)?
What size was the breast tumour?
Was the skin covering it of natural colour (if not, what was the colour?)?
Was there any ulceration in the skin covering the tumour or was the skin whole?
Was there any pain in the breast tumour?
Was it tender to the touch? Had the same breast sometimes felt tender prior to the appearance of the tumour (when?)?
Did the mamilla of the diseased breast bleed, either of itself or when pressed? Did it exude any other fluid (what kind?)?
Had the same breast bled prior to the appearance of the tumour (when?)? or exuded any other fluid (what kind?)?
Were any enlargements (lymph nodes) felt in the armpit on the side where the tumour was located?
Has the other breast sometimes been swollen (when?) or tender (when?)?
Did you put on or lose weight while you had the tumour in the breast (how much?)? What was your height and weight at the time of operation? What are they now?
Did you take any medicine in the months preceding the appearance of the breast tumour (what? how much?)?
Has the breast tumour recurred after operation (if so, when, and how was it treated?)?
Have you had other tumours since the operation on the breast tumour (what? where? when?)?
Are you at present in good health, or are you ill (how?)?

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Photomicrographs

Photo 1. Carcinoma solidum alveolare. x 30. Haematoxylin-eosin. M. 2391.

Photo 2. Adenocarcinoma. x 120. Haematoxylin-eosin. G-ck.

Photo 3. Carcinoma solidum medullare. x 100. Haematoxylin-eosin. X 4411.

Photo 4. Carcinoma Paget. x 380. Haematoxylin-eosin. 542 -45.

Photo 5. Carcinoma scirrhosum. x 380. Haematoxylin-eosin. S. 14068.

Photo 6. Carcinoma basocellulare. x 100. Haematoxylin-eosin. S. 4539.

Photo 7. Fibrosarcoma. x 190. Haematoxylin-eosin. 222 -43.

Photo 8. Carcinoma spinocellulare. x 250. Haematoxylin-eosin. S. 3460.

Photo 9. Fibrosarcoma. x 250. Haematoxylin-eosin. P-on.

Photo 10. »Mantle connective tissue» — ; eosinophilic secretion with a couple of desquamated cells. x 30. Haematoxylin-eosin. S. 16041.

Photo 11. Lobulus (same as in Photo 12.); acini; »mantle connective tissue» + . x 30. Haematoxylin-eosin. X 3131.

Photo 12. Lobuli; »mantle connective tissue» + ; eosinophilic secretion. x 20. Haematoxylin-eosin. X 3131.

Photo 13. »Mantle connective tissue» + . x 20. Haematoxylin-eosin. M. 6362.

Photo 14. General view of gynecomastia with »mantle connective tissue» + . x 20. Haematoxylin-eosin. V-k.

Photo 15. Epithelial proliferation. x 250. Haematoxylin-eosin. 3547 -47.

Photo 16. Epithelial proliferation. x 250. Haematoxylin-eosin. V-k.

Photo 17. Papilloma in a small duct. x 190. Haematoxylin-v. Gieson. S. 9322.

Photo 18. »Pale epithelium». x 500. Haematoxylin-eosin. 1135 -45.

Photo 19. »Intermediate epithelium». x 500. Haematoxylin-eosin. 1135 -44.

Photo 20. »Intermediate epithelium». x 500. Haematoxylin-v. Gieson. Kir. 580/1923 N-m.

Photo 21. »Pale» and ordinary epithelium in the same duct; abundant inflammation cell infiltration. x 190. Haematoxylin-v. Gieson. 1364 -47.

Photo 22. »Pale» and ordinary epithelium in the same duct. x 190. Haematoxylin-v. Gieson. 1987 -46.

Photo 23. »Pale», »intermediate» and ordinary mammary gland epithelium in the same duct. x 380. Haematoxylin-eosin. M. 8484.

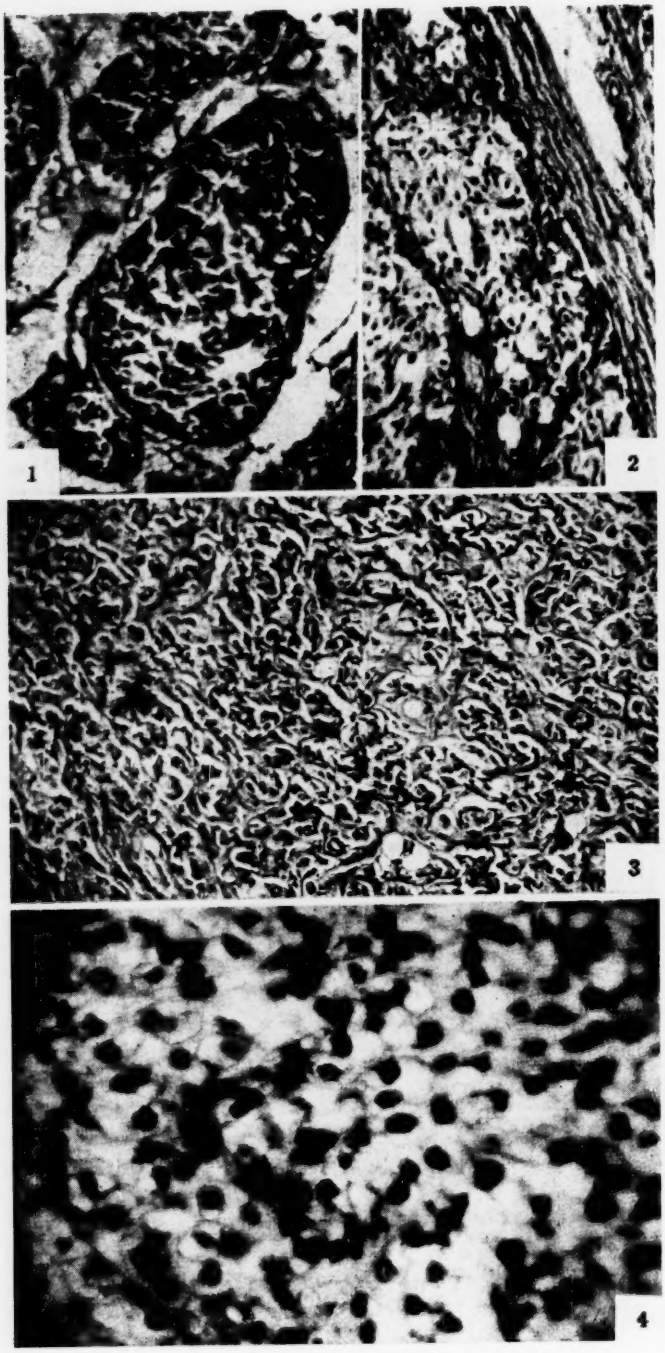
Photo 24. »Pale» and »intermediate» epithelium in the same duct. x 190. Haematoxylin-eosin. 3293 -47.

Photo 25. A cyst containing eosinophilic cell-free secretion; apocrine secretion. x 190. Haematoxylin-eosin. M. 6954.

Photo 26. A cyst containing acidophilic secretion and desquamated epithelial cells. x 190. Haematoxylin-v. Gieson. S. 9322.

Photo 27. Cysts containing basophilic secretion and a few desquamated epithelial cells; apocrine secretion. x 190. Haematoxylin-eosin. M. 6954.

Photo 28. Apocrine sweat glands and an ordinary sweat gland containing basophilic secretion. x 190. Haematoxylin-eosin. M. 6954.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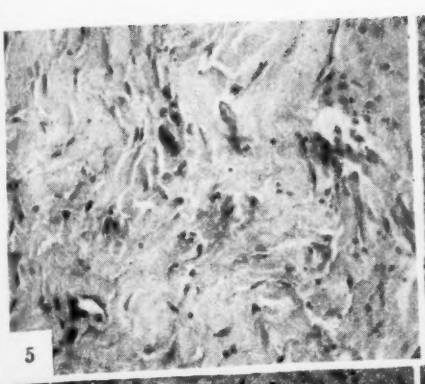

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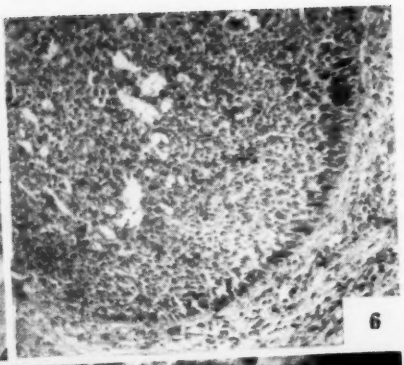

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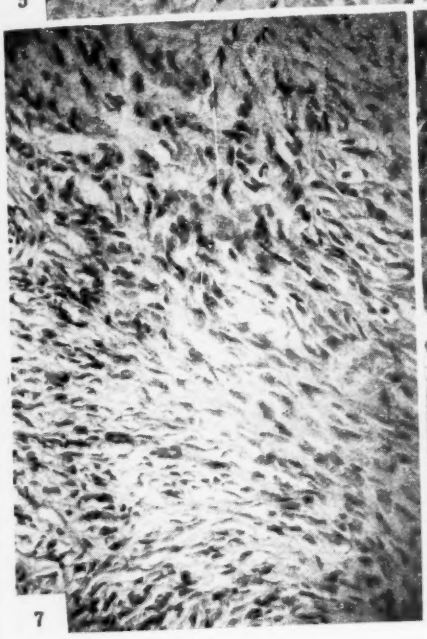

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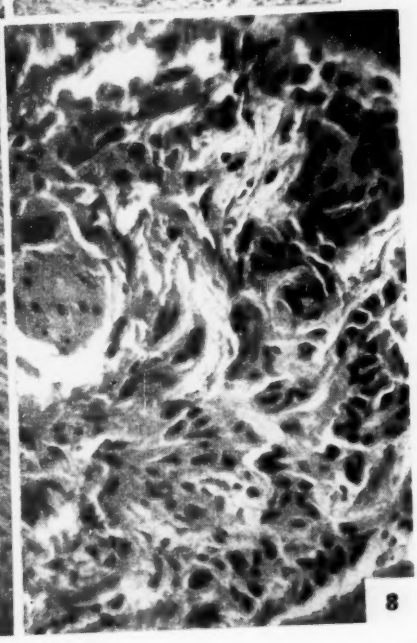

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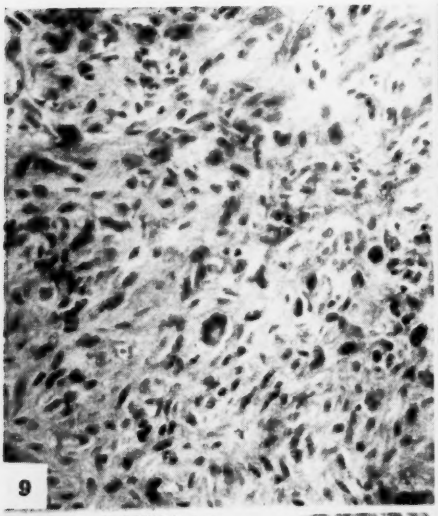

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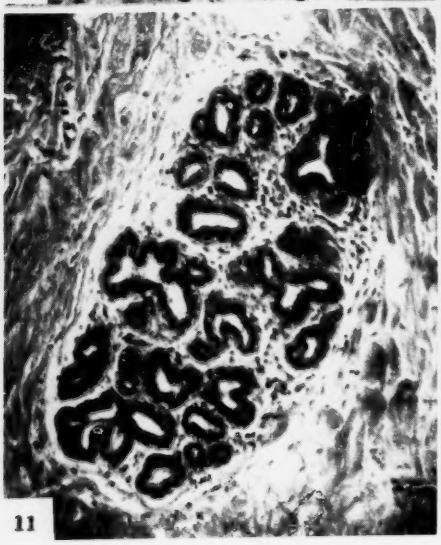

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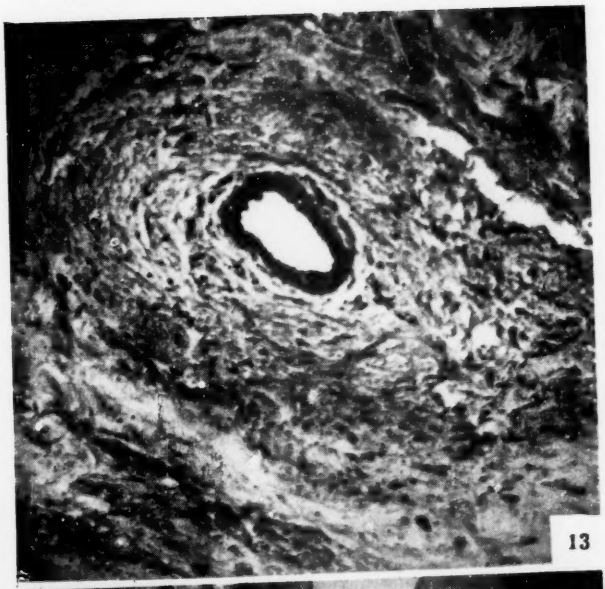
12



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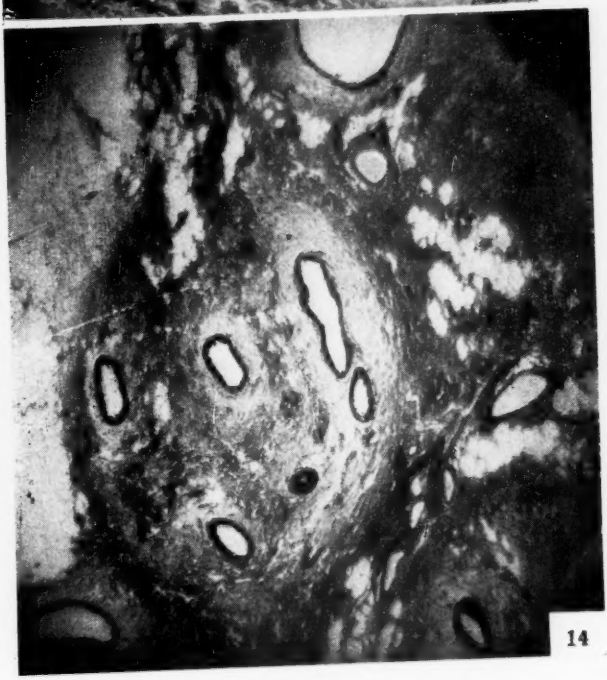

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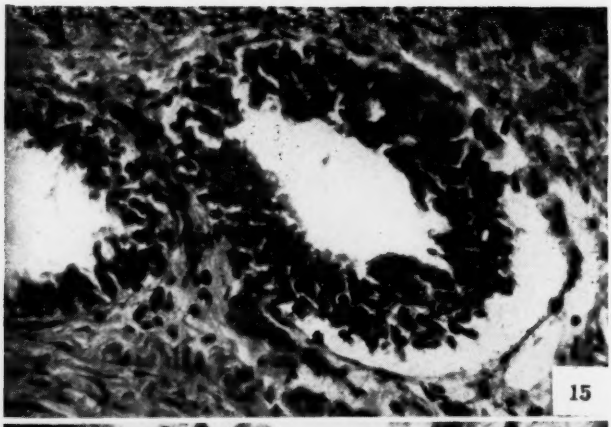

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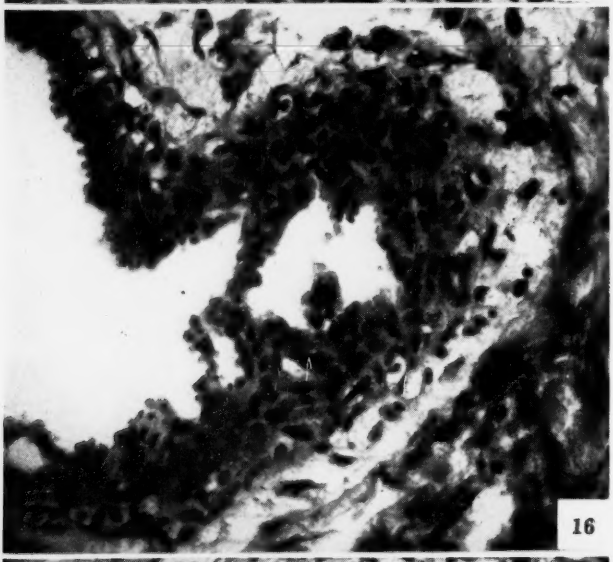

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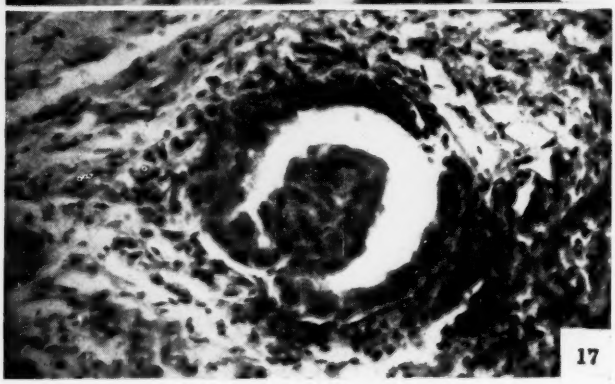
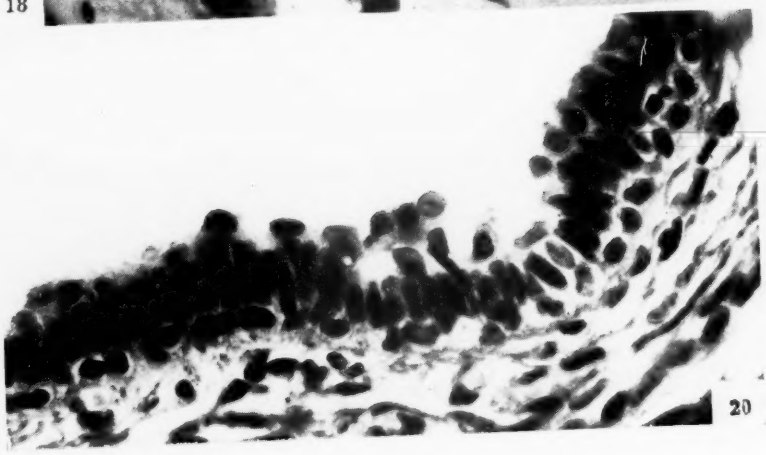


17

18

19



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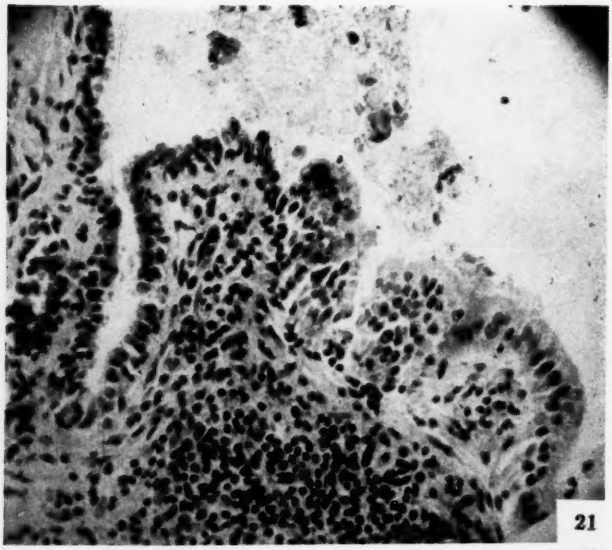

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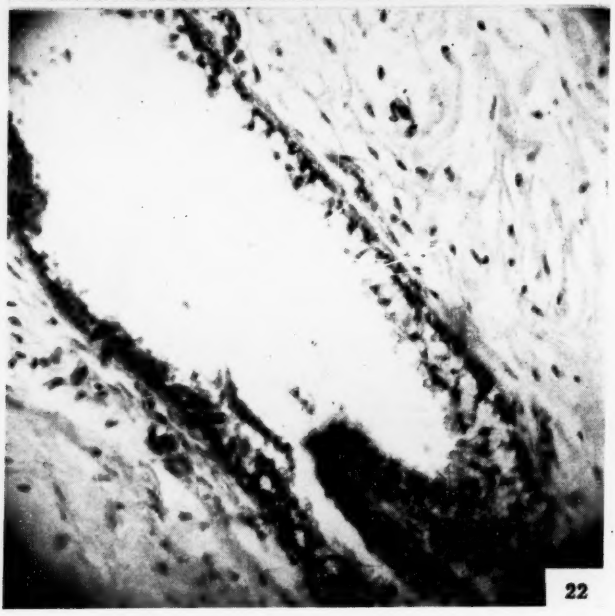


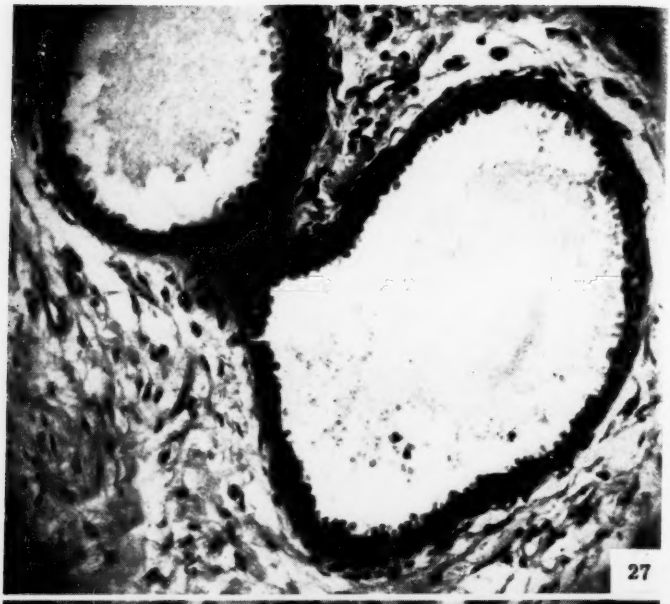
22

23

24

25

26



27

28

INDEX

Vol. 29